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BEHAVIOR OF THE SYSTEMIC BLOOD PRESSURE, PULSE RATE AND SPINAL FLUID PRESSURE

ASSOCIATED WITH ACUTE CHANGES IN INTRACRANIAL PRESSURE ARTIFICIALLY PRODUCED

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In a previous paper [1] it was indicated that many of the commonly employed hypotheses concerning the physiologic factors at work in a patient suffering from an acute expanding lesion of the intracranial cavity are open to challenge. The historical development of these hypotheses was traced, and specific attention was called to the wide disparities of opinion among present day surgeons concerning the diagnosis, prognosis and treatment of trauma to the brain. In an attempt to account for the existence of such widely differing views among those of apparently equal authority, it seemed to us that a considerable degree of responsibility might be referred to the almost universal acceptance some thirty years ago of certain principles which had their origin in animal experimentation [2] and to the persistent effort on the part of the

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1. Browder, J., and Meyers, R.: Observations on Behavior of the Systemic Blood Pressure, Pulse and Spinal Fluid Pressure Following Craniocerebral Injury, Am. J. Surg. **31**:403, 1936.

2. (*a*) Duret, H.: Recherches anatomiques sur la circulation de l'encephale, Arch. de physiol. norm. et path. **1**:2, 60, 316, 664 and 919, 1874; (*b*) Notes sur la physiologie pathologique des traumatismes cérébraux, Gaz. med., Paris **6**:5, 599, 612 and 624, 1877; (*c*) Etudes expérimentales et cliniques sur les traumatismes cérébraux, Thèse de Paris, no. 63, 1878. (*d*) von Bergmann, E.: Allgemeine traumatisch bedingte Störungen des endocraniellen Nervensystems, in von Billroth, T., and Luecke, G. A.: Deutsche Chirurgie, Stuttgart, F. Enke, 1880, no. 30, p. 266; (*e*) Die Lehre von den Kopfverletzungen, in von Billroth, T., and Luecke,

(Footnote continued on next page)

clinician to interpret cases in human beings directly in terms of these principles. The principles referred to are recapitulated here.

1. Agents that produce rapid cerebral compression, provided they are intense enough to raise the general intracranial pressure so that the external tension on the medulla oblongata is equal to the diastolic or to the mean systemic arterial blood pressure, will produce: (*a*) a steady rise in blood pressure to above normal; (*b*) a steady decrease in pulse rate to below normal, the pulse being characterized by a bounding ("vagal") quality; (*c*) slow, deep and stertorous respirations, becoming Cheyne-Stokes in character; (*d*) vomiting; (*e*) headache, and (*f*) mental torpor, stupor and, later, coma.

2. From the pathogenic standpoint, these effects are the direct result of two factors which in any given case may act independently of each other or concomitantly: (*a*) ischemia of the vital medullary centers and of the brain generally, and (*b*) a local fall in the blood pressure of these structures, brought about by the partial or complete occlusion of the arterioles of the brain under the influence of the rising intracranial pressure. The early effect of the forces of external compression on the walls of the vessels is to increase the local blood pressure. As the external pressure increases and the lumen of the vessel is narrowed, the force of the axial stream becomes lessened, both relatively and absolutely, and the shearing resistance of the peripheral stream against the wall of the vessel becomes greater, with a resulting dissipation of the mechanical energy imparted to the blood stream by the heads of pressure (i. e., the heart and the elastic rebound of the arteries). As a consequence, the blood pressure falls in those tissue beds supplied by the compressed arterioles.

3. Death is preceded by a progressive increase in intracranial pressure, a decrease in systemic blood pressure, a racing pulse and respiratory collapse.

G. A.: Deutsche Chirurgie, Stuttgart, F. Enke, 1880, no. 30, p. 341. (*f*) Hill, L.: Physiology and Pathology of the Cerebral Circulation, London, J. & A. Churchill, 1896, p. 168. (*g*) Kocher, T.: Hirnerschütterung, Hirndruck und chirurgische Eingriffe bei Hirnerkrankungen, in Nothnagel, H.: Specielle Pathologie und Therapie, Vienna, A. Hölder, 1901, vol. 9, p. 2. (*h*) Cushing, H.: Concerning a Definite Regulatory Mechanism of the Vasomotor Centre Which Controls Blood Pressure During Cerebral Compression, Bull. Johns Hopkins Hosp. **12**:290, 1901; (*i*) Some Experimental and Clinical Observations Concerning States of Increased Intracranial Tension, Am. J. M. Sc. **124**:375, 1902; (*j*) Blood-Pressure Reaction of Acute Cerebral Compression, Illustrated by Cases of Intracranial Hemorrhage, ibid. **125**:1017, 1903. (*k*) Cooper, A.: Lectures on the Principles and Practice of Surgery, London, T. & G. Underwood, 1894, vol. 1, pp. 282-313. (*l*) Eyster, J. A. E.; Burrows, M. T., and Essick, C. R.: Studies on Intracranial Pressure, J. Exper. Med. **2**:489, 1901. (*m*) Eyster, J. A. E.: Blood Pressure Changes in Cheyne-Stokes Respiration, Bull. Johns Hopkins Hosp. **17**:296, 1906.

These principles, while they represent valid deductions from the conditions of animal experimentation, did not seem to us justifiably applicable to the actual clinical material, because when a series of severe uncomplicated cases of trauma to the brain were studied and the measure of the objective vital signs recorded we observed none to be wholly consistent with the classically described findings. Moreover, we were unable to find any close similarity between our records and that modification (fig. 2) of the original schema of the animal experimenters which has been proposed by certain clinicians.[3] For these reasons we found ourselves unable to subscribe to certain long held interpretations relative to cases of injury to the brain of the sort studied; namely, (1) that the essential and clinically important effect of intracranial trauma

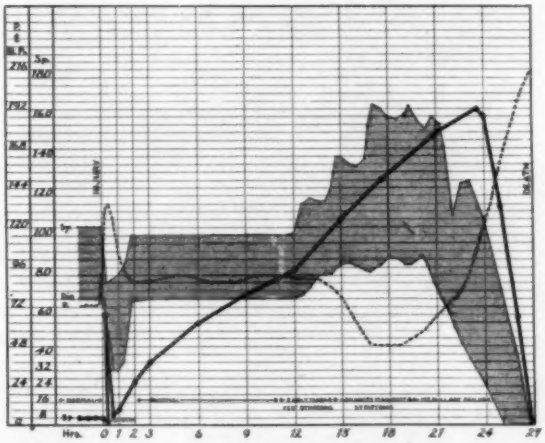

Fig. 1.—Chart illustrating the course of events following a rise in intracranial pressure according to the experimental findings in animals, as noted by Kocher, Cushing, Eyster and others. After recovery from the initial shock, as the progressive increase in intracranial pressure is established, no change is imposed on the blood pressure and pulse rate until the intracranial pressure becomes equal to the diastolic and/or mean arterial pressure. When these levels are reached the blood pressure rises and the pulse rate falls. With increasing embarrassment, medullary failure appears and collapse becomes clinically evident.

is the production of increased intracranial pressure; (2) that increasing intracranial pressure produces its vital effect through stimulation of the medullary centers; (3) that the estimation of certain of these effects (increased blood pressure, decreased pulse rate, slow, deep respirations, stupor, etc.) enables one to deduce ipso facto that intracranial pressure

3. Bailey, Pearce: Diseases of the Nervous System Resulting from Accident and Injury. New York, D. Appleton & Co., 1906, p. 44.

is on the increase and (4) that death results from overstimulation of the medullary centers under the influence of a steadily rising intracranial tension.

In order to bring the question of the alleged constitutional effects of increased intracranial pressure fairly under inquiry, this factor alone, uncomplicated by any other intracerebral factors (such as may be presumed to obtain following severe trauma to the head), should be the object of study. As was noted in the previous paper of this series, it is uncommon clinically to find cerebrospinal fluid pressures as high as from 40 to 70 mm. of mercury (from 540 to 950 mm. of water), and only rarely are higher levels encountered. In the present study, as a supplement to our clinical observations in cases of injury to the brain, an attempt was made to determine experimentally in human beings the

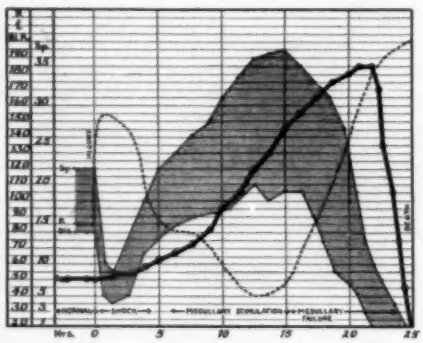

Fig. 2.—Chart illustrating the course of events following a rise in intracranial pressure according to a conception widely employed and taught in surgical practice. After recovery from the initial shock, the intracranial pressure rises and there is a pari passu rise in the blood pressure and fall in pulse rate until medullary failure ensues. From this point on the blood pressure falls, the pulse races and shock becomes evident, leading almost inevitably to death.

effect on the vital signs that could be produced by raising the intracranial tension to levels of a magnitude equal to or higher than the levels in cases of the most severe trauma.

MATERIAL AND METHOD

Ten patients, each of whom had a large operative cranial defect, were used for the observations. At the time of the study, each patient had convalesced from an exploratory operation for tumor of the brain, and it was readily possible, through the cranial defect (fig. 3), to influence the intracranial contents by the application of agents of external pressure. For purposes of control, comparable studies were carried out on three patients with intact craniums.

The standard procedure consisted in placing the patient horizontally in bed in the lateral prone position. The subject was made to lie so that the side of the

cranial defect was uppermost. He was left in this position for from one-quarter to one-half hour, or until his vital readings reached a constant level. A sphygmomanometric cuff was placed about the head and strapped with adhesive tape in such a manner as to cover completely the region of the cranial defect. A second cuff was secured in place about the arm of the uppermost side, and a stethoscope was led away from the cubital fossa. A no. 18 gage spinal needle was passed into the lumbar thecal sac and appropriately connected with the adapter of a spinal manometer. (In some instances a mercury spinal manometer was employed; in others, a water manometer.) A few minutes after the introduction of the spinal

Fig. 3.—Patient C. M., with a bulge at the site of the decompression. Through this cranial opening the intracranial pressure was readily influenced by strapping a sphygmomanometric cuff about the head and inflating the cuff so as to attain the desired pressure.

needle the initial control reading was made. In the interest of facility and simultaneous recording, the experimental set-up required an operator and two assistants. It was the task of the operator to attend to the hand bulb controlling the pressure on the head. The first assistant kept time for the group and noted the respirations and also the pulse rate. The second assistant read the blood pressure and checked on the pulse rate. Rhythmic team-work was easy to establish, and notations were rapidly recorded on a previously plotted form (fig. 4).

EXPERIMENTAL STUDIES

The salient clinical features derived from a study of four of the thirteen patients [4] used for these experiments, together with the tables and graphs derived from the corresponding experimental data, are briefly reviewed here.

In the graphs the abscissa represents the time, and each unit interval equals one minute. In the first ordinate column may be read the pulse rate (P.) and blood pressure (Sy, Dia.) levels. Each unit represents five beats per minute, or 5 mm. of mercury, as the case may be. In the second ordinate column are read the respiratory rate (Resp.), the head

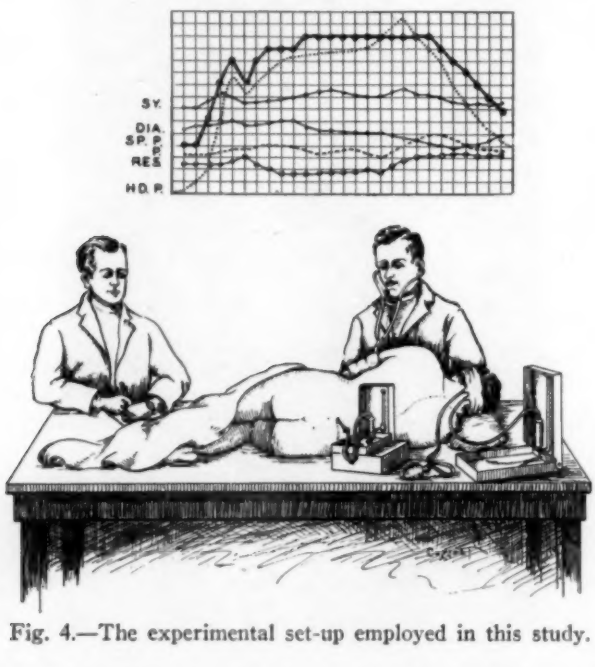

Fig. 4.—The experimental set-up employed in this study.

pressure (Hd.P.) and the cerebrospinal fluid pressure (Sp.P.) levels. The unit intervals here represent three respirations per minute, or 3 mm. of mercury, as the case may be. The curve of the pulse rate is represented by a heavy broken line. The curves for the systolic (Sy.) and diastolic (Dia.) blood pressures are in heavy black dots connected by uninterrupted narrow lines. They constitute the boundaries of a gray band which may be regarded as the pulse pressure. The curve for the respiratory rate is represented by circles and dashes, that for the

4. The data on the remaining patients have been omitted from this communication in the interest of conciseness of presentation. In their essential features, the principles illustrated in these experiments conform closely to those illustrated in the four experiments recorded here.

cerebrospinal fluid pressure by a continuous heavy black line and that for the head pressure by closely spaced dots.

It is obvious that the absolute head pressure curve has no dynamic significance in these experiments, as its magnitude in any given instance is determined by (*a*) the size of the cranial defect, (*b*) the position of the cranial defect and (*c*) the cerebrospinal fluid pressure it was desirable to produce experimentally in that case. It did seem requisite, however, to record the level of pressure exerted against the head, so that comparable pressures might be employed in performing the control experiments.

Experiment 1 is a representative example of the three control experiments. The condition of two of the patients was diagnosed as a paroxysmal convulsive disorder, and that of the third patient was diagnosed as osteo-arthritis of the spine. It seemed desirable that these control experiments should be made lest the criticism be raised that the prolonged pressure of the headcuff on the scalp, affecting as it does the capillary and venous beds over a relatively wide area, might influence the general circulation [5] in such a way as to equivocate the findings presented in those experiments in which the changing intracranial pressure was under study.

EXPERIMENT 1.—H. L., a white woman aged 21, was admitted to the Bellevue Hospital on Oct. 10, 1934, because of recurring episodes of unconsciousness. Three months prior to admission she had had a severe headache for from three to four hours, followed by a giddy feeling, involuntary jerkings of the right upper extremity and, finally, a period of unconsciousness of about ten minutes' duration. During the next two weeks she was unusually drowsy and slept a great deal. When the drowsiness passed off, she complained that both hands felt numb and that the righf leg seemed stiff. Four such attacks occurred up to the time of her admission. The results of the physical, neurologic and laboratory examinations were negative. Encephalography revealed nothing unusual in either the subarachnoid space or the ventricular system. The Queckenstedt test was negative. A diagnosis of a paroxysmal convulsive disorder of undetermined etiology was made. The data for this experiment are presented in table 1 and figure 5.

The patient stated that she felt "nervous" at the start of the experiment. She complained about the head pressure between the twenty-fifth and the fortieth minute but was cooperative throughout.

The foregoing record illustrates the variation in vital signs which may be expected in a control subject under conditions of the experimental set-up.

EXPERIMENT 2.—C. M., a 40 year old Italian woman, was admitted to the Kings County Hospital on May 13, 1934. In October 1930 she had undergone

5. L. Kubie, in discussing the paper of Stevenson, Christenson and Wortis at the 1929 meeting of the Association for Research in Nervous and Mental Diseases, raised just such a question concerning the physiologic effects of the pressure band.

an operation elsewhere for the removal of a tumor of the right temporal lobe. For the succeeding two and one-half years she remained fairly free from symptoms. However, two months before her admission to the Kings County Hospital, headache, drowsiness, dizziness and defects in memory appeared and increased progressively. Vomiting occurred at times, and periods of stupor alternated with those of a lucid state. Physical examination revealed a deeply stuporous, well

TABLE 1.—*Data for Experiment 1*

Time, Min.	Head Pressure, Mm. of Hg	Spinal Pressure, Mm. of Hg*	Pulse Rate, per Min.	Blood Pressure, Mm. of Hg	Respiratory Rate, per Min.
Control	0	8.0	104	112/68	18
1	60	7.8	118	110/66	18
3	70	8.0	106	110/68	17
5	80	8.0	100	114/62	17
7	90	8.2	96	108/62	18
9	100	8.0	96	106/64	16
12	110	7.8	96	110/66	15
15	120	7.0	98	114/62	14
20	120	7.5	100	112/60	16
25	120	7.5	104	114/72	17
30	120	6.8	100	116/64	18
35	120	8.0	88	108/60	18
40	120	8.0	96	114/64	17
45	120	8.2	100	110/66	16
50	120	7.8	104	112/62	16
55	120	8.0	94	110/64	16
60	120	7.5	92	108/64	16
65	0	7.5	88	110/66	18

* A water manometer was used. The figures were translated into mercury equivalents for the purpose of uniformity of record.

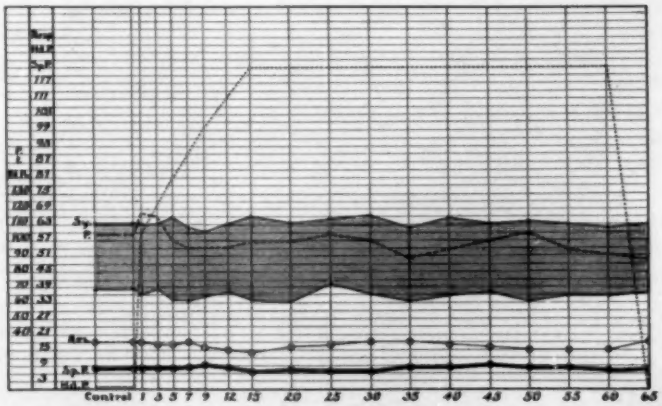

Fig. 5 (case 1).—Record of a patient with a paroxysmal convulsive disorder. This record is representative of the control group and illustrates the variations in vital signs that may be expected under conditions of the experiment.

developed and well nourished woman in early middle life. A bulging mass the size of a large plum presented within the omega-shaped operative scar on the right side of the head. Bilateral exophoria was noted, and there were slow lateral oscillations of the eyes. The pupils were equal and reacted sluggishly. Ophthalmoscopy revealed bilateral papilledema of a high degree. The abdominal reflexes were absent. There was paresis of a suprasegmental type on the left side, with a fairly sustained ankle clonus on the left and an equivocal Babinski sign on the

same side. The deep reflexes were generally overbrisk. Sensory examination was unsatisfactory because of the mental state. After twenty-four hours on a dehydrating regimen, the patient became bright and oriented. At this time it was evident that she suffered a moderate degree of amblyopia and anesthesia on the left side. Her mental acuity varied from then on until reoperation on May 17. At this time an infiltrating tumor, fully as large as a lemon, was found occupying the usual site of the right temporal lobe and insula Reili and going deep ventrally across the floor of the middle fossa to the region of the right crus cerebri. The tumor was removed except for a small tag of tissue, which either actually invaded

TABLE 2.—*Data for Experiment 2*

Time, Min.	Head Pressure, Mm. of Hg	Spinal Pressure, Mm. of Hg*	Pulse Rate, per Min.	Blood Pressure, Mm. of Hg	Respiratory Rate, per Min.
Control	0	20	112	110/ 84	24
1	10	28	...	111/ 85	24
2	14	30	110	130/ 95	26
3	18	36	104	130/ 95	24
4	22	38	98	128/ 90	24
5	..	..	...	.....	..
6	30	45	112	128/ 96	26
7	34	50	96	125/ 95	26
8	..	..	...	.....	..
9	40	53	108	128/ 96	26
10	42	55	108	130/ 92	24
11	44	58	110	130/ 98	27
12	46	58	108	128/ 98	26
13	50	60	104	126/ 95	26
14	52	62	104	.....	24
15	52	64	104	122/ 96	24
20	52	61	104	122/100	27
25	52	59	104	120/ 98	22
30	52	58	106	124/ 94	20
35	52	57	102	128/ 92	21
40	52	56	100	119/ 92	22
45	52	56	106	124/ 95	22
50	52	54	102	128/ 95	22
55	52	54	100	126/ 96	21
60	52	53	102	122/ 94	18
65	52	52	97	125/ 93	18
70	52	51	96	124/ 96	16
75	52	49	92	127/ 97	17
80	52	47	100	123/ 98	18
85	52	46	98	126/ 99	18
90	52	44	..	126/100	18
95	52	42	98	.....	20
100	52	41	96	126/ 96	20
105	52	40	98	.....	18
110	52	38	96	125/ 95	18
115	52	36	88	126/ 97	19
120	52	35	98	127/ 94	20

* A mercury manometer was used.

or was strongly attached to the right crus. At the end of the procedure a large decompression opening was left, the bone flap being sacrificed. Recovery was uneventful. There was marked improvement in the sensory and motor disparities, in visual acuity and in the mental state. Three weeks after operation the site of the decompression was bulging prominently and proved fluctuant on palpation. Aspiration yielded 147 cc. of a thin, clear, sterile, straw-colored fluid. Within two weeks the bulge had recurred to its previous size and as before was attended by headache. Aspiration at this time revealed what appeared to be a clear, colorless cerebrospinal fluid. Figure 3 shows the bulging zone over which the cuff of the sphygomanometer was strapped in the experimental study. The patient was discharged on July 25 and is at present being seen regularly in the outpatient clinic. The data for this experiment are presented in table 2 and figure 6.

The patient was quiet and conscious throughout the entire two hours of observation. There was no headache or drowsiness and no notable mental or nervous symptoms.

The cerebrospinal fluid pressure in this experiment was slowly elevated to a level higher than that encountered clinically, the purpose being to simulate a relatively slow collection of blood in the intracranial cavity. After the level of 64 mm. of mercury was reached, the head pressure was kept constant, and the slow compensatory change in spinal fluid pressure was recorded. At no time did the systemic blood pressure or pulse rate undergo a significant change. The systolic pressure did not exceed 130 mm. of mercury, and the pulse rate did not become slower than 92 per minute. Only at the beginning of the experiment did a slight change in the systemic blood pressure supervene. This may have been ascribable to emotional factors,[6] for it did not continue to rise pari passu with the progressive rise in the cerebrospinal fluid pressure.

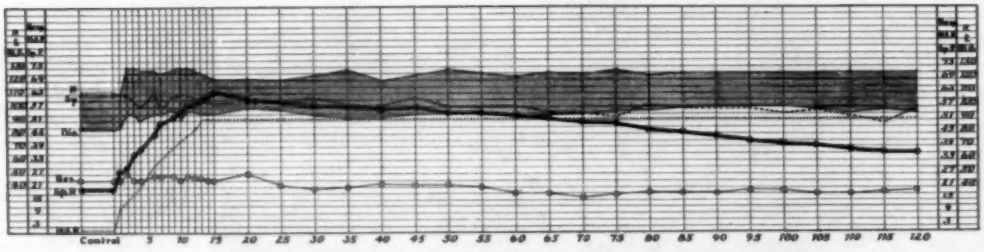

Fig. 6 (case 2).—Postoperative record of a patient with a glioma of the right temporal region. It will be noted that although the intracranial pressure was elevated to 64 mm. of mercury and was kept at a higher than clinical level for well over an hour, the blood pressure at no time rose to a clinically significant level and the pulse rate showed no tendency to bradycardia.

Moreover, the interpretation of this slight rise in blood pressure in terms of an emotional state receives support in that no corresponding

6. (*a*) Pavlov, I.: Scientific Study of the So-Called Psychical Processes in the Higher Animals, in Lectures on Conditioned Reflexes, translated by W. H. Gantt, London, Martin Lawrence, Ltd., 1928; (*b*) Principle Laws of the Activity of the Central Nervous System as Shown from the Study of Conditioned Reflexes: Interaction of Centres, Russk. Vrach **11**:1507, 1912; (*c*) The Objective Study of the Highest Nervous System Activity, in Lectures on Conditioned Reflexes, translated by W. H. Gantt, London, Martin Lawrence, Ltd., 1928, p. 213; (*d*) The Pure Physiology of the Brain, in Lectures on Conditioned Reflexes, translated by W. H. Gantt, London, Martin Lawrence, Ltd., 1928, p. 241. (*e*) Nikolaev, P. N.: Analysis of Complex Conditioned Reflexes, Arch. d. sc. biol. **16**:411, 1911. (*f*) Stroganov, V. V.: Development of a Conditioned Reflex to, and Differentiation of, Compound Stimuli, in Sbornik Pavlova, Leningrad, 1925. (*g*) Babkin, B. P.: Contributions to the Problem of the Relative Strengths of Conditioned Stimuli, Proc. Russian Med. Soc. **78**:1, 1911.

elevation of systemic blood pressure appeared when the second study was carried out on this patient (see table 3 and fig. 5), even though in this instance a much more severe and prompt rise in cerebrospinal fluid pressure was employed. It may be held that the emotional response related to the strangeness of the experimental set-up had largely passed off at the time of the second observation.

EXPERIMENT 2 a.—A. M., the same subject used in experiment 2, was observed a second time. The effect of an almost instantaneous rise (i. e., within thirty seconds) of the cerebrospinal fluid pressure was the matter chiefly under study. This observation was carried out two days after the first experiment, and the data are presented in table 3 and figure 7.

TABLE 3.—*Data for Experiment 2 a*

Time, Min.	Head Pressure, Mm. of Hg	Spinal Pressure, Mm. of Hg*	Pulse Rate, per Min.	Blood Pressure, Mm. of Hg	Respiratory Rate, per Min.
Control	0	20	116	118/78	28
½	52	73	112	128/84	30
1½	52	68	111	125/82	30
2	..	..	...	.....	..
2½	..	..	...	.....	..
3	52	65	104	122/84	28
4	52	62	110	124/85	28
5	52	60	107	116/88	30
6	..	..	...	.....	..
7	52	58	106	188/88	28
8	52	57	108	122/88	28
9	52	56	110	120/86	27
10	52	55	108	122/84	26
11	..	..	...	.....	..
12	..	..	...	.....	..
13	52	52	106	121/82	30
15	52	52	110	119/82	30
20	52	46	114	119/86	25
25	52	43	114	124/88	26
30	52	41	104	118/85	25
35	52	38	102	128/96	24
38	34	33	110	128/92	25
30	34	32	110	126/86	25
40	20	23	96	122/90	24
43	20	23	106	125/94	24
45	0	13	106	118/88	22
50	0	13	102	119/84	23

* A mercury manometer was used.

The patient was feeling irritable and restive. She made no verbal complaint, but at times (starting at the twenty-fifth minute) grunted at the end of expiration and expressed impatience with the procedure.

In this experiment the effect of a sudden rapid and high rise of cerebrospinal fluid pressure was studied. No significant change in the systemic blood pressure, pulse rate or respiratory rate was observed.

EXPERIMENT 3.—J. W., a white man aged 52, was transferred to the Bellevue Hospital on March 12, 1935, from another hospital, where his condition was diagnosed as glioblastoma multiforme in the left frontotemporal region. The earliest symptoms had appeared two years before admission and consisted of transient recurrent paralysis of the right upper extremity. In December 1934 he had an episode of transient aphasia of the receptive and emissive type. Except for these symptoms, the patient felt well and was able to work until Jan. 10, 1935,

at which time the aphasia became so severe that he was required to give up his position. Dizziness and headache on the left side appeared in a few days. All symptoms progressed steadily from this time on, until a left subtemporal decompression was performed late in February 1935. No attempt was made to remove the tumor. A small specimen was removed for histologic study. This was diagnosed as glioblastoma multiforme. Physically, the patient presented the facies of one chronically ill, but otherwise he was well developed and well nourished and was mentally alert. Except for the neurologic picture, the results of the general examination were unimportant; on admission the systolic blood pressure was 132 mm. of mercury, and the diastolic pressure was 84 mm. of mercury. A large soft swelling presented over the left temporal region. The operative scar was well healed. A marked receptive and emissive aphasia was apparent, and the language defect interfered with the carrying out of a refined neurologic examination. Ophthalmoscopic examination revealed bilateral papilledema and evidences of old and recent retinal hemorrhages. Nystagmus was elicited on lateral gaze to right and left. Paresis, deep hyperreflexia and hypesthesia were demonstrable on the right side. The abdominal reflexes were absent on the right.

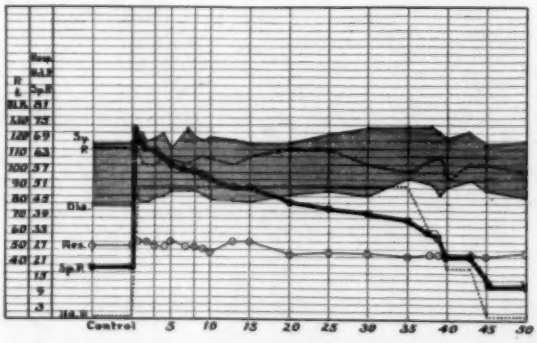

Fig. 7 (case 2 a).—Postoperative record of a patient with a glioma of the right temporal region. In the face of a sudden rapid and high elevation of the intracranial pressure, the blood pressure, the pulse rate, the respiratory rate and the state of consciousness remained essentially unaffected.

A Babinski sign was elicitable on this side. The results of the laboratory studies of the blood and urine were reported as negative. Three days after admission, the patient became stuporous, but otherwise his condition remained fair and the stupor cleared after a therapeutic lumbar puncture. Two days later the experimental observations recorded in table 4 and figure 8 were made.

Throughout the entire procedure the patient was mildly stuporous. Except for frequent moans, he engaged in no active motor protest. There appeared to be no further depression of his state of consciousness during the course of the experiment.

This experiment illustrates an elevation of the cerebrospinal fluid pressure to a level appreciably higher than that met clinically. Moderate changes in the systemic blood pressure were observed, the maximum systolic level being 150 mm. of mercury, whereas the diastolic pressure at this time was 64 mm. of mercury. These observations are quite in keeping with those which have been recorded in experiments on animals.

At one period bradycardia occurred, but singularly enough the blood pressure was falling at this time, even though the cerebrospinal fluid pressure was being increased. Again, at the time when the systolic blood pressure reached its highest level (150 mm. of mercury), no tendency toward bradycardia was evident, the pulse rate being 80 per minute. It is to be noted that the diastolic pressure was exceeded by the intracranial pressure between the twentieth and the sixty-fifth minute of the experiment.

TABLE 4.—*Data for Experiment 3*

Time, Min.	Head Pressure, Mm. of Hg	Spinal Pressure, Mm. of Hg*	Pulse Rate, per Min.	Blood Pressure, Mm. of Hg	Respiratory Rate, per Min.
Control 1	0	34	88	108/74	14
Control 3	0	34	88	108/74	14
Control 5	0	35	88	110/70	14
1	28	56	84	110/78	14
2	62	80	84	114/78	14
3	60	80	84	120/92	18
4	54	70	96	130/90	18
5	84	92	96	134/92	18
6	80	90	88	130/84	18
7	84	92	68	126/88	20
8	90	102	48	126/80	20
9	88	84	40	122/62	18
10	88	80	43	102/58	20
11	88	78	48	102/58	20
12	84	78	44	104/58	22
15	88	80	60	106/56	16
20	88	82	68	134/58	20
25	88	80	68	122/68	20
30	88	78	78	124/58	22
35	88	81	74	124/58	20
40	88	76	80	134/60	18
45	88	76	78	130/60	18
50	106	86	72	134/60	18
55	106	88	72	134/60	18
60	106	86	80	140/60	18
65	106	86	76	150/64	18
70	50	68	68	132/60	18
72	50	66	68	132/60	20
75	20	50	80	130/56	20
85	8	40	78	135/50	22
90	8	40	78	134/50	24
95	0	28†	72	130/54	24
100	0	20‡	80	132/60	24
105	0	12#	84	132/56	24

* A mercury manometer was used.
† Fifteen cubic centimeters of cerebrospinal fluid was withdrawn.
‡ Five cubic centimeters of cerebrospinal fluid was withdrawn.
# Four cubic centimeters of cerebrospinal fluid was withdrawn.

EXPERIMENT 4.—B. A., a 39 year old white housewife, was admitted to the Kings County Hospital on Dec. 4, 1935, complaining of generalized headache, bilateral tinnitus, vomiting and progressive paresis on the left side of several months' duration. Thirteen years previous to admission she had been institutionalized for hebephrenic schizophrenia, the symptoms of which were irregularly present until the onset of her headaches. Examination revealed an oriented but distractable and at times incoherent patient with grandiose delusions, facetiousness and periodic psychomotor acceleration. Visual acuity was diminished. The visual fields could not be properly tested, but marked papilledema was present bilaterally. The left pupil was larger than the right. Paresis involving the left side of the face and the left arm and leg was evident. This was attended by the usual signs

of disease of the upper motor neurons, including hyperreflexia, ankle clonus and a Babinski sign. Sensation and coordination proved to be within normal limits. The results of the usual laboratory studies were negative, and the vital signs and the roentgenograms of the skull were normal. Ventriculography disclosed evidence of a tumor mass compressing the body of the right lateral ventricle from above and somewhat posteriorly. At operation on December 10 a right parieto-occipital bone flap was turned down, and a subcortical tumor of soft, spongy, vascular, infiltrating type was encountered. All evident tumor tissue was sucked away. Histologic examination revealed the tumor to be a glioblastoma. The bone flap was removed at the close of the operation. After this procedure, the postoperative course was satisfactory, and two weeks later the personality symptoms were much improved. Three months later the observations recorded in table 5 were made. At this time evidence of recurrence of the tumor had presented itself, and the site of the decompression was bulging. The patient continued without change until June 1936, after which her status slowly became vegetative and she became progressively worse, dying seven and one-half months after operation. The data for this experiment are presented in table 5 and figure 9.

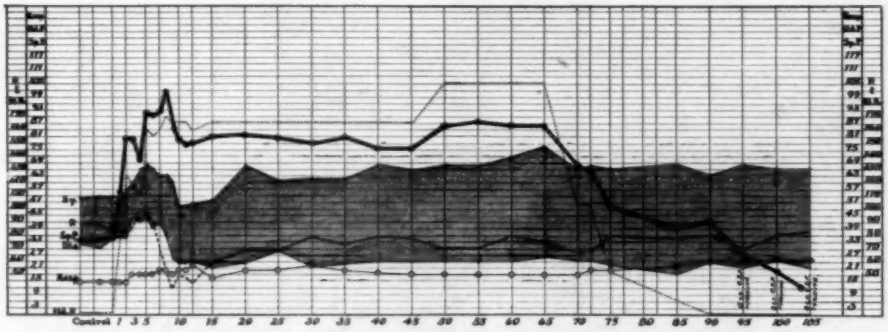

Fig. 8 (case 3).—Postoperative record of a patient with glioma of the frontotemporal region. The interesting feature of this record is the fall of systemic blood pressure attending an increase in cerebrospinal fluid pressure. It will be noted also that during this same period bradycardia became evident.

The patient was conscious and alert, offering no complaint until the twenty-seventh minute, when she said that her "heart hurt." When the cerebrospinal fluid pressure reached 130 mm. of mercury, she became restive and complained of headache, then lost consciousness momentarily. Immediately after this she became mentally clear and offered no complaint. At the thirty-sixth minute, when the cerebrospinal fluid pressure was elevated to 140 mm. of mercury, the face became flushed, the pupils dilated and the respiration rapid and snorting, and in addition undue motor activity appeared. The patient was incontinent. Stupor was of only moderate degree, and a few verbal responses were obtainable. Continuation of high cerebrospinal fluid pressure during the next four minutes resulted in deeper stupor, marked sweating and the appearance of a striking cutaneous erythema. A few slight convulsive twitches occurred. As indicated in table 5, a constant level of high cerebrospinal fluid pressure was difficult to maintain. On the graph the average cerebrospinal fluid pressure during these periods is plotted as a broken line. Reduction of the cerebrospinal fluid pressure to a level of 80 mm. of mercury resulted in an improved state of consciousness. The cutaneous homogeneous blush

TABLE 5.—*Data for Experiment 4*

Time, Min.	Head Pressure, Mm. of Hg	Spinal Pressure, Mm. of Hg*	Pulse Rate, per Min.	Blood Pressure, Mm. of Hg	Respiratory Rate, per Min.
Control 1	0	32	118	118/ 92	16
Control 2	0	30	102	110/ 92	16
5	36	82	106	122/ 92	16
7	38	84	102	116/ 90	16
12	35	80	92	118/ 86	14
17	38	80	108	128/ 90	16
22	42	80	86-100	132/ 92	16
27	60	94	98	122/ 90	16
29	94	130	120	154/102	16
31	50	82	98	140/ 96	12
34	60	88	89	130/ 90	12
36	120	112-140	..	.....	Rapid snorting
39	108	126-136	140	184/118	18
40	111	120	136	168/118	20
43	114	120	144	182/118	18
44	64	80	66	128/ 84	18
46	66	82	....	.....	..
51	74	84	118	140/ 96	16
52	134	114-120	146	188/120	22
56	128	112-118	92	172/108	18
57	0	26	60	122/ 86	14
60	0	28	..	.....	..
62	0	21	68	108/ 78	12
65	0	20	68	100/ 74	12
70	0	20	76	100/ 74	14

* A mercury manometer was used.

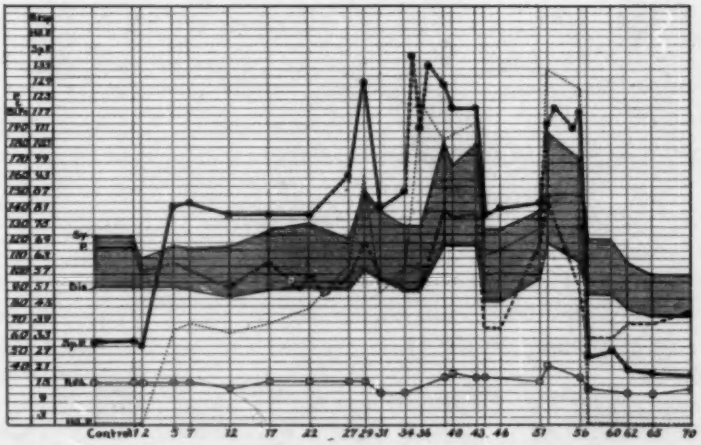

Fig. 9 (case 4).—Postoperative record of a patient with glioblastoma multiforme of the right parieto-occipital lobe. In this record the curve representing the cerebrospinal fluid pressure has been broken corresponding to periods during which the patient became restive and her respirations irregular. At these times the fluctuations of the cerebrospinal fluid pressure were so rapid as to preclude their being separately represented on the graph. However, the limits within which variations occurred are here indicated. It will be noted that the findings associated with intracranial pressure levels above 100 and 110 mm. of mercury are consistent with those reported in animal experimentation. Below these levels, only slight variations in systemic blood pressure, pulse rate and respiratory rate appeared.

at this time changed to a mottled pattern. Elevation of the cerebrospinal fluid pressure again to a level between 110 and 120 mm. of mercury led to stuporousness, restiveness and snorting respirations. Toward the end of the experiment, when the pressure on the head was released, responsiveness was regained and the restiveness abated.

Only slight changes were imposed on the systemic blood pressure, pulse rate, respiratory rate and state of consciousness until the cerebrospinal fluid pressure was raised to a level of 110 mm. of mercury. A matter of considerable interest is noted in that in this patient elevation of the cerebrospinal fluid pressure to levels high enough to affect the systemic blood pressure resulted in a rise of the latter attended by an increase in the pulse rate rather than the classically expected decrease. Again, when the cerebrospinal fluid pressure was released, the blood pressure rather promptly returned to its previous level and the pulse rate slowed down unduly. Finally, this experiment represents another instance in which intracranial pressure exceeded the diastolic blood pressure.

COMMENT

A critical examination of the records obtained on human beings with operative cranial defects indicates that within the limits of the present experimental conditions no striking alterations are imposed on the systemic blood pressure and pulse rate by increasing the cerebrospinal fluid pressure to levels equal to and considerably exceeding (from 60 to 140 mm. of mercury) those clinically encountered in cases of trauma to the brain (from 10 to 60 mm. of mercury). Only in those instances in which the cerebrospinal fluid pressure was raised to an unusually high level was there an appreciable response on the part of the systemic blood pressure and the pulse rate, and that was not necessarily in accord with the classic pattern. These observations coincide with a slowly accumulating body of evidence, scattered throughout the literature of the past quarter of a century,[7] to the effect that there is no relationship between

7. (*a*) Solomon, H. C.: The Effect on Human Cerebrospinal Pressure of Extraction and Injection of Fluid, A. Research Nerv. & Ment. Dis., Proc. **5**:82, 1927. (*b*) Weed, L. H.: Studies on Cerebrospinal Fluid: II. Theories of Drainage of Cerebrospinal Fluid with an Analysis of Methods of Investigation, J. M. Research **31**:21, 1919; (*c*) Studies on Cerebrospinal Fluid: III. The Pathways of Escape from the Subarachnoid Spaces with Particular Reference to the Arachnoid Villi, ibid. **31**:51, 1919; (*d*) Cerebrospinal Fluid, Physiol. Rev. **2**:171, 1922. (*e*) Forbes, H. S.; Fremont-Smith, F., and Wolff, H. G.: Resorption of Cerebrospinal Fluid Through the Choroid Plexus, Arch. Neurol. & Psychiat. **19**:73 (Jan.) 1928. (*f*) Fremont-Smith, F., and Merritt, H. H.: Relationship of Arterial Blood Pressure to Cerebrospinal Fluid Pressure in Man, ibid. **30**:1309 (Dec.) 1933; (*g*) The Relationship of Cerebrospinal Fluid Pressure to Systolic Blood Pressure, J. Nerv. & Ment. Dis. **78**:291, 1933. (*h*) Fremont-Smith, F., and

(Footnote continued on next page)

cerebrospinal fluid pressure and systemic blood pressure unless the level of the former reaches the diastolic or mean blood pressure. Thus, Fremont-Smith and Merritt,[7f] in a study of 1,606 cases, found that the levels of the diastolic and the systolic blood pressure were uninfluenced in the face of intracranial pressure up to 800 mm. of water and that the cerebrospinal fluid pressure was uninfluenced in the face of increased vascular tension by itself. These observations agreed with results published in a previous paper by Fremont-Smith and Kubie.[7h] A number of investigators who have carried out experiments with animals had been led to similar conclusions (Becht,[7j] Cushing,[2j] Eyster,[21] Wolff and Forbes,[7m] Weed and Hughson,[7n] Becht and Matill [7o]), and as a result of their clinical and experimental observations, Adson and Lillie,[7q] Parker,[7r] Gurdjian [7s] and Wilson [7p] have been able to lend their support to the same expression. Yet despite the lines of evidence advanced by these authors, the majority of practitioners continue to be guided by the notion that a rise in cerebrospinal fluid pressure per se to levels of the magnitude met in clinical practice regularly affects the systemic blood pressure and the pulse rate. According to the observations made after craniocerebral injuries, which were reported in our previous paper, the relationship between variables, viz., cerebrospinal fluid pressure, systemic blood pressure, respiratory rate and pulse rate, may assume any pattern mathematically possible. Although it may occasionally appear that the reaction on the part of the blood pressure and the pulse rate to a rapidly expanding intracranial lesion (brain trauma) conforms to the Kocher pattern, it would rarely, if ever, prove on mensuration of the cerebrospinal fluid pressure to be explicable in terms of this factor alone. This does not mean to imply that the reduction of even a mild increase in the measurable intracranial tension may not in certain instances influ-

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Kubie, L.: The Relations of Vascular Hydrostatic Pressure and Osmotic Pressure to the Cerebrospinal Fluid Pressure, A. Research Nerv. & Ment. Dis., Proc. **8**:7, 1927. (*i*) Shelbourne, S. A.; Blain, D., and O'Hare, J. P.: The Spinal Fluid in Hypertension, J. Clin. Investigation **11**:489, 1932. (*j*) Becht, F. C.: Studies on Cerebrospinal Fluid, Am. J. Physiol. **51**:1, 1920. (*k*) Cushing.[2j] (*l*) Eyster, Burrows and Essick.[21] (*m*) Wolff, H. G., and Forbes, H. S.: The Cerebral Circulation, Arch. Neurol. & Psychiat. **20**:1035 (Nov.) 1928. (*n*) Weed, L. H., and Hughson, W.: Systemic Effects of the Intravenous Injection of Solutions of Various Concentrations with Especial Reference to the Cerebrospinal Fluid, Am. J. Physiol. **58**:53, 1921. (*o*) Becht, F. C., and Matill, P. M.: Studies on the Cerebrospinal Fluid, ibid. **51**:126, 1920. (*p*) Wilson, A. A.: Blood Pressure Observations in Tumors of the Brain, Arch. Neurol. & Psychiat. **28**:891 (Oct.) 1932. (*q*) Adson, A. W., and Lillie, W. I.: The Relationship of Intracranial Pressure, Choked Disc and Intraocular Tension, Tr. Am. Acad. Ophth. **30**:138, 1927. (*r*) Parker, W. R.: The Relation of the Tension of the Eyeball to the First Appearance of Papilledema, A. Research Nerv. & Ment. Dis., Proc. **8**: 256, 1927. (*s*) Gurdjian, E. S.: Studies on Acute Cranial and Intracranial Injuries, Ann. Surg. **97**:327, 1933.

ence the systemic blood pressure and the pulse rate. Our interpretation, however, has been that certain less obvious but none the less real factors consequent on craniocerebral trauma, and loosely spoken of as cerebral edema, fluid imbalance, intramolecular derangement, etc., are the prime determinants of the objective clinical manifestations in any given case. That these in turn may be modified to a degree by factors of intracranial pressure is reserved as a definite and plausible probability, especially since at times the reduction of pressure favorably influences the patient's clinical course.

A point that seems to be worthy of final notice is that whereas an increase in intracranial tension within the limits of clinical experience may not effect a rise in systemic blood pressure, the statement is not intended to deny that such an increase of intracranial tension may produce a rise in cerebral blood pressure. That the latter can and regularly does occur appears to have been clearly demonstrated within the past five years. The groundwork for this was laid when the old doctrine of the passivity of cerebral blood vessels was disproved and the point established in 1928 by Forbes and his co-workers [8] that the circulation of the brain is controlled in part by specific cerebral vasomotor nerves. Tournade in 1921 had reason to postulate the existence of a regulating mechanism for the cerebral circulation.[9] Recent experimental and clinical studies of the circle of Willis and of the retinal arteries have amply demonstrated the point that increase of the intracranial tension is attended by parallel increase of blood pressure within the cerebral vessels.[10]

CONCLUSIONS

1. Within the limits of this series of experiments general support is lent to the findings of certain animal experimentalists who have dealt with intracranial problems, i. e., that increases in intracranial pressure below the level of mean systemic arterial pressure have no effect on the pulse rate, respiratory rate or systemic blood pressure. On the other hand, our findings do not agree with those of the experimentalists who have advanced the view that the "compensatory rise" in blood pressure

8. Forbes, H. S., and Wolff, H. G.: Cerebral Circulation: III. The Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928.

9. Tournade, A.; Chabrol, M., and Marchand, H.: Des mécanismes nerveux régulateurs de la pression artérielle: I. La régulation centrale, Compt. rend. Soc. de biol. **84**:610, 1921. Tournade, A.: Des mécanismes nerveux régulateurs de la pression artérielle: II. Sa mise en jeu par l'hypotension aortique, ibid. **84**:723, 1921.

10. Berens, C.; Smith, H. T., and Cornwall, L. H.: Changes in the Fundus and in the Blood Pressure in the Retinal Arteries in Increased Intracranial Pressure, Arch. Neurol. & Psychiat. **20**:1151 (Dec.) 1928. Adson and Lillie.[7q] Parker.[7r]

is such as to keep the diastolic blood pressure above the level of the intracranial pressure. We have several times observed a rise of intracranial tension up to and above that of the diastolic pressure without its imposing a significant change on the systemic blood pressure.

2. As pressures of the magnitude used in the present experiments are rarely approached in clinical cases of injury to the brain, it seems defensible to reiterate here the point previously made in our traumatic studies, namely, that the classic conception of the sequence and course of events supervening in cases of "rapidly increasing intracranial pressure," and consisting of a steady rise in blood pressure to above normal, a steady fall in pulse rate, a decrease in respiratory rate, a rise in temperature and stupor, coma and vomiting, has practically no application in clinical cases.

3. We are further unable to substantiate the clinical converse of this classic conception to the effect that from a study of systemic blood pressure, pulse, respiration and the state of consciousness, either alone or in combination, one may reliably infer that intracranial tension is increasing or decreasing.

4. In our experience, repeated observations on the cerebrospinal fluid pressure by themselves cannot be employed as an index of the clinical condition of the patient, of his likely course or of the necessity for surgical intervention.

5. "Increased intracranial pressure producing medullary paralysis" can rarely be regarded as the prime responsible factor leading to death in cases of injury to the head.

ABDOMINAL ADHESIONS AND THE USE OF PAPAIN

A DISCUSSION AND AN EXPERIMENTAL STUDY

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In 1935 I began an experimental study relative to abdominal adhesions, which work when completed encompassed data obtained from certain clinical observations and from 145 operations or autopsies on 55 animals.[1] Since permanent abdominal adhesions were created in a number of these animals, I decided to use some of them for investigating the efficacy of papain as a preventive of the reformation of adhesions. Accordingly, an analysis of relevant data obtained from the foregoing work was correlated with additional experimentation with papain.

To evaluate the data in this paper properly, it is necessary to review briefly the history of proteolytic ferments as they have been used in attempts at prevention of adhesions. A number of investigations in this regard have been made in the last twenty-five years relative to the prophylactic or curative value of pepsin, trypsin and papain. Some investigators have felt that the first two substances were of value. More recent work has indicated that a solution of papain is more stable, less irritating in supposedly effective concentrations and less likely to be inactivated by intra-abdominal fluids than pepsin and trypsin. Consequently, the investigation of papain has become at this time more popular than that of other proteolytic enzymes. Kubota[2] studied it, and Ochsner and his co-workers have been chiefly responsible for its consideration in this country. Walton has done considerable work with this substance and believes it to be valuable. In one series of experiments Ochsner and Garside, using 280 animals, reached the conclusion that a solution of papain was 90.89 per cent effective in preventing the reformation of freshly divided preexisting adhesions.[3]

From the Department of Surgery, University of Arkansas School of Medicine.

1. Donaldson, J. K.: A Study Regarding Abdominal Adhesions and of Cotton and Gauze Sponges, Am. J. Surg., to be published.

2. Kubota, T.: Prevention of Peritoneal Adhesions, Japan M. World **2**:226 (Aug.) 1922.

3. Ochsner, A., and Garside, Earl: Peritoneal Adhesions: Their Prevention by Use of Digestive Ferments, Surg., Gynec. & Obst. **54**:338 (Feb.) 1932.

Ochsner and Storck later gathered and reported data referring to its clinical use by 24 different surgeons, including themselves. In this series it was used prophylactically, or to prevent the reformation of adhesions, in 231 cases.[4] In 37 of these cases subsequent operations were performed, thereby allowing observation as to the effectiveness of the solution of papain which had been instilled at a previous operation. Fausel[5] concluded that papain was effective in preventing the formation of adhesions when it was used prophylactically. He did not believe that it would dissolve previously formed adhesions, and he did not experiment with it to prevent the reformation of divided ones. Bogart recently published an article in which he concluded that papain in a solution of 0.08 per cent sodium citrate in distilled water is of value in preventing adhesions.[6] Grieco[7] apparently alone sounded a discordant note in his study of papain. He concluded that it was of no value.

Previous workers have had difficulty getting the prepared powdered papain into solution. Grieco experienced this trouble. He found papaiotine, a refined constituent of papain, soluble in water and a weakly active digestant. He believed, however, that it was ineffective in preventing postoperative abdominal adhesions, as was papain in his hands. Bogart expressed the belief that sodium citrate assists in dissolving the prepared papain. He did not discuss the pharmacology or chemistry of this action.

EXPERIMENTAL METHODS AND RESULTS

The method I used to produce adhesions was found satisfactory for my purposes in that its effects were fairly constant quantitatively and in that it presented little chance for divergence in technic. It simply consisted of attaching by a single silk stitch sterile gauze pledgets, approximately 1.75 by 1.75 by 0.13 cm., to the large intestine on each side of the entrance site of the small bowel, care being taken not to perforate the wall of the intestine with the stitch. Gauze sponges left here for five days or more and then removed left a consistent and fairly constant degree of abrasion, which invariably formed permanent adhesions to adjacent parts after the pledgets were removed. By this method one may instil the solution of papain at the time the sponges are removed and obtain some idea as to its prophylactic value, or else one may allow permanent adhesions to form, separate them, instil the solution and study its efficacy in preventing their reformation.

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4. Ochsner, A., and Storck, A.: Prevention of Peritoneal Adhesions by Papain, Ann. Surg. **104**:736 (Oct.) 1936.

5. Fausel, E. G.: Experimental Postoperative Intraabdominal Adhesions, M. Times & Long Island M. J. **62**:1 (Jan.) 1934.

6. Bogart, L. M.: Intra-Abdominal Adhesions: An Experimental and Clinical Study, Arch. Surg. **34**:129 (Jan.) 1937.

7. Grieco, F.: Experimental Research on Prevention of Postoperative Peritoneal Adhesions: Use of Papain, Ann. ital. di chir. **13**:269 (March 31) 1934.

Investigation in this series was confined mostly to the latter procedure. It has been well proved previously that separated adhesions of the intestine will recu in almost 100 per cent of the cases to at least the same degree and extent as previously existed if nothing is done to prevent it. I used 10 animals as controls, however, separating adhesions which had been previously established by the foregoing method. In these animals the adhesions recurred in about 100 per cent to the same degree and extent as previously.

The papain used was obtained in two different consignments. The first consignment was obtained in the late fall of 1935 and was used shortly after it was received. An attempt was made to place it in solution by Ochsner's method of emptying the sterile prepared powder into a sterile mortar and grinding the powder with a pestle in a quantity of Hartman's solution. The solution or suspension of papain was used promptly after it was prepared. The time which it was kept in solution or suspension before its use within the abdominal cavity is noted in the table. The experiments were carefully controlled under aseptic conditions. The second quantity of papain was obtained in the late fall of 1936 directly from the company and was used within a few days. It was prepared essentially in the same way as the first consignment but in Ringer's solution. The first quantity of powder was more granular than the second. The second consignment was a finer powder, which quite easily went into suspension or solution. I feel that there is some question as to whether either consignment of the drug was completely soluble. Both times the preparations were made there remained throughout the solution fine white granules or flakes which unquestionably were simply suspended. The results of the experiments and further details regarding their character are noted in the table. All operative procedures and interpretations on the animals listed in the table were done by me in order that there would be no chance for personal variations in the procedures and readings. My observations were confirmed. The second consignment of papain was also used promptly after being prepared. The abdominal cavities of the animals listed in the table were practically or completely filled with the solution of papain in a concentration of 1 : 50,000. Rabbits were used exclusively. Care was used in closing the suture lines, and it was felt that all of them were leak proof. Postoperative observations by attendants revealed no leakage. As is noted in the table, I was not able to prove that papain had any effectiveness in this series.

In 5 additional animals (not included in the table) papain, 1 : 50,000, prepared in Hartman's solution was used prophylactically. The substance was instilled into the cavity of each animal at the time the sponges were removed and before definite permanent adhesions had been established. No prophylactic effectiveness was demonstrated. I have discarded any definite interpretation in this group because the suspension or solution of the papain used had been prepared for from one to several days before instillation. According to Walton's tables the solution had, however, been kept at a temperature which for the length of time it was kept should have rendered it from 40 to 70 per cent effective when it was used. The quantities used in this group were somewhat less than were necessary to fill the cavities completely.

In attempting to classify adhesions, a grading of from 1 to 4 was used. Adhesions of grade 2 or 3 were almost invariably produced by leaving the sponges in for five days. In one or two of the animals the sponges were left in longer before they were removed, and in one or two others, perforation of the intestine was caused by removal of the sponges. In the latter animals somewhat more extensive adhesions were formed than in those in which the sponges had

been left in place only five days and in which no perforation of the intestine occurred during removal of them. In animal 17 the bowel was perforated at the time the permanent adhesions were separated, and some gross contamination occurred. The perforation was repaired with black silk, and the solution of papain was instilled into the cavity. It may be noted that the animal recovered and that the degree of adhesions at autopsy were interpreted as being of at least the same grade as they were originally. In other words, as far as I can tell the papain did not prevent desirable formation of adhesions in the presence of infection and as far as I know had no beneficial action. In the group of 5 animals in which the weaker papain preparation was used, some of the latter substance was instilled at the time perforation of a bowel was procured. Recovery occurred with the formation of strong adhesions.

Results of Experiments on Animals With Papain

Animals Serial No.*	Degree of Adhesions Separated	Papain, 1:50,000, in Hartman's or Ringer's Solution, Cc.	Length of Time in Suspension or Solution Before Use	No. of Days Before Killing Animal	Degree of Adhesions at Autopsy
34	Grade 3	22	2 hr. 15 min.	30	Grade 3
32	Grade 2	15	30 min.	30	Grade 2
30	Grade 1½	25	1 hr. 15 min.	30	Grade 1½
29	Grade 3	25	2 hr. 20 min.	30	Grade 2
25	Grade 3	25	2 hr.	30	Grade 3
24	Grade 2	25	45 min.	30	Grade 3½
14	Grade 2	35	5 min.	36	Grade 2
15	Grade 3½	40	40 min.	36	Grade 3½
16	Grade 2	25	2 hr. 20 min.	14 Died in fight	Grade 2½
18	Grade 3½	25	1 hr.	36	Grade 3½
17	Grade 4	65	1 hr. 30 min.	60	Grade 4

* The 1935 consignment of papain was used for the first six animals; the 1936 consignment for the latter five.

ANALYSIS

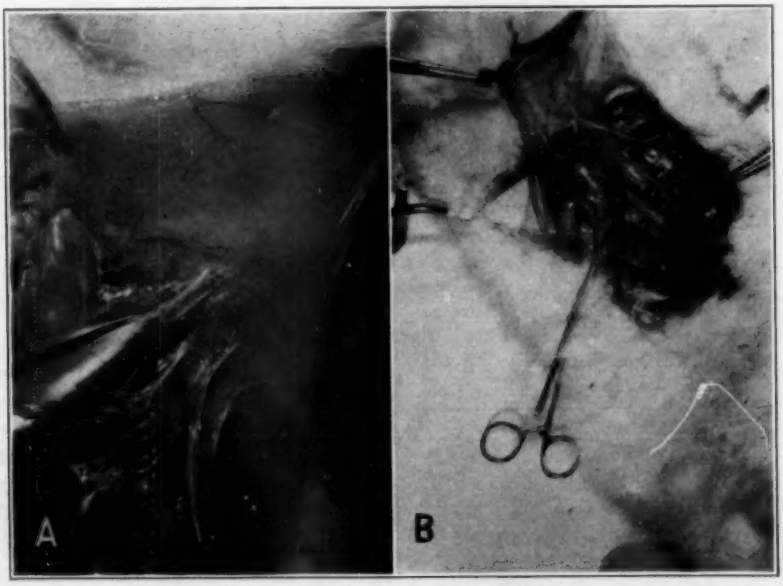
As stated previously, a review of the literature to date regarding the use of a solution of papain to prevent the formation of adhesions reveals that the majority of investigators who have used it have felt it to be of value. Grieco and I seem to be alone in having obtained completely unsatisfactory results with the drug.

In order to arrive at conclusions as to the value of papain as indicated in the experiments and observations made by the workers listed, a careful analysis is necessary. In this analysis one should take into consideration the following:

1. The size of experimental and clinical series.
2. The methods used in the production of adhesions together with the accuracy and number of control experiments.
3. The methods used in the observation and interpretation of results.
4. The consistency of results obtained.
5. The chances of error in the preparation and administration of the drug and its inherent potentially variable characteristics, such as stability and solubility.

Nearly all who have worked with papain in connection with adhesions have produced the adhesions by the method developed by Ochsner and his co-workers. This consists of rubbing the bowel in the ileocecal region with gauze until the intestine is considered sufficiently irritated or abraded and then applying tincture of iodine to the irritated area. Several investigators have attested to the fact that adhesions may be produced by this method.

Of the workers named, Ochsner and his associates have the largest experimental and clinical series. In their last study, in which observations were made by 24 different surgeons on 231 different patients, the 37 patients who were subsequently reoperated on obviously offered



A, a typical picture of the reformation of adhesions which occurred in the animals after the use of papain. Note the adhesions between the intestinal loops themselves as well as those attaching the loops to the parietal peritoneum. The adhesions shown here are somewhat more extensive than those created by simply leaving the sponges in situ for five days. *B*, moderate adhesions as they reformed between the intestinal loops themselves as well as to the parietal peritoneum after the instillation of papain. These are more or less typical of those which are formed by leaving the sponges in situ for five days, and the photograph shows the typical results listed in the table.

the best opportunity for an accurate interpretation of results. The number of surgeons among whom this group of 37 patients was divided was not mentioned in the article. One could presume that a number of different surgeons made observations on a limited number of the patients. In some respects this would be advantageous and

in other respects disadvantageous. Ochsner and Storck stated that of the 37 patients, 32 had massive adhesions which, according to reports, did not reform after the instillation of a solution of papain.

A word as to Ochsner's method of producing adhesions. He and his co-workers used ample controls. Presumably others have felt confident regarding their own application of his procedure. I believe that investigators using this method, however, should take certain precautions in applying it and in interpreting the results. In a previous attempt to establish some method of measurement of the amount of trauma required to produce adhesions by rubbing gauze across the small intestine, I was surprised to find the degree of violence which was necessary.[1] This statement concurs with the conclusions of Hertzler, who stated that the degree of violence necessary to produce adhesions by rubbing the wall of the intestine with gauze is generally considerably underestimated. Others have mentioned the difficulty of consistently producing experimental abdominal adhesions. In my past experience with friction by means of gauze, an actual tear or gross denudation of the serosa was necessary. Simple hyperemia of the intestine produced by rubbing is not sufficient to produce permanent adhesions. Likewise I have seen the intestine become rather heavily and widely tainted with tincture of iodine without adhesions subsequently forming. This is not necessarily a criticism of the method under discussion but a declaration as to the necessity of one keeping the foregoing points in mind. It is obviously desirable to be as quantitatively consistent as possible in the production of adhesions in these studies, particularly when a small series of animals is used as has been the case with the majority of investigators on this subject.

Fausel used 10 animals guarded by 10 controls.

Bogart studied 38 rabbits in his experiments as well as 30 patients. He divided the 38 rabbits so that he could study 14 different types of solutions and methods of producing adhesions. The largest number of rabbits in which he apparently used exactly the same type of technic was 6. In these he seems to have used the Ochsner method of irritation followed promptly by the instillation of his own solution of sodium citrate and papain. He concluded that adhesions were completely prevented in 4 and that only thin ones were present in the other 2. He also concluded that in 3 animals papain in distilled water was of limited prophylactic value. In 3 animals he divided the adhesions and instilled the solution of sodium citrate and papain. One of these died the first day. In the other 2 moderate adhesions of the bowel to the wound were present on the twentieth day. The remainder of his experimental studies were rather varied. No definite side by side controls seem to have been used. He reported good results in 22 of 30 patients in whom

papain had been used either prophylactically or after the division of adhesions. Only 2 of the series seem to have been subsequently operated on by Bogart. There was 1 patient in whom he instilled the papain solution into the abdomen simply for the purpose of dissolving the adhesions. He said that he produced good clinical results in this instance, but subsequent operation allowing inspection of the treated cavity was not afforded.

Grieco's work, as far as I know, was carefully done and, as stated previously, he felt that papain had no value as a preventive of the formation of adhesions. His results in this work were evidently consistent.

My series of experiments reported here is small as compared to those of Ochsner and his co-workers. The results in 5 of the 26 animals considered as directly belonging to this series should not be evaluated except to a limited extent. The remaining 21 were operated on with careful technic, and apparently a fresh solution of papain, prepared from the fresh powdered sterile drug put up in 25 mg. packages, was used. Six additional animals which inopportunely died are not considered in the series. My results were very consistent, and I feel that the method that I used in producing the adhesions had the advantage of presenting little chance for error in application. It produces adhesions that are quite uniform in nature, location and quantity, thereby affording accurate controls and perhaps enhancing the value of a smaller series of animals.

Walton [8] and others expressed the belief that they have sufficiently established the fact that the powdered papain prepared by the method being used by the company furnishing this drug remains active for considerable lengths of time. It is not difficult to carry out the methods recommended for placing this substance in solution. It has been established, however, that after the substance is placed in the solutions recommended it apparently loses its effectiveness fairly rapidly. It is fair to assume that all the aforementioned investigators have made no errors in their technic of preparation and administration. It is also assumed that all investigators have either made their readings themselves or else have felt that they could depend on readings made by others.

One other point regarding the possible misinterpretation as to the reformation of adhesions should be mentioned. It is not of particular consequence but could conceivably give rise to some error. When adhesions to an old incision line are separated it is sometimes possible to prevent or limit their return at this particular site by proper closure of the peritoneum. The raw surfaces on the parietal peritoneum along

8. Walton, R. P.: Behavior of Papain in Peritoneal Cavity, J. Pharmacol. & Exper. Therap. **43**:487 (Nov.) 1931.

the incision following the division of the adhesions are sometimes everted in such a way as to obliterate them from the cavity. The visceral parts of the adhesions separated from this area will usually find attachment unless something is done to prevent it but may do so elsewhere than at the site of the suture line. Their absence from the suture line might simply mean a change of location and not prevention of recurrence.

COMMENT

It would seem to me that careful analysis indicates that the value of papain in preventing the formation of adhesions has not as yet been thoroughly established. Further proof of the consistent stability and solubility of papain would seem desirable before it can be accepted. Furthermore, considerably more investigative work with methods for the production of adhesions, which are as consistent and as free from error as possible and which are thoroughly understood by each individual experimenter, are advisable.

CONCLUSONS

1. In a series of 26 animals I was unable to demonstrate that papain was effective in preventing the reformation of adhesions.

2. A brief review and an analysis of past work on papain are given.

Dr. Paul L. Day, of the Department of Chemistry of the University of Arkansas, assisted in preparing and administering the papain and in reading the results. Capt. Leonard Heaton, formerly of the Fort Sam Houston Hospital, also assisted in part of the readings.

Parke, Davis & Co. prepared the consignments of papain.

DISEASE OF THE MESENTERIC LYMPH NODES

ITS RELATION TO APPENDICITIS, GASTRO-INTESTINAL INFECTIONS AND GENERALIZED DISEASES; REPORT OF ONE HUNDRED AND TWENTY-THREE CASES; POSSIBLE ETIOLOGY AND TREATMENT

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The purpose of this article is to consider first the mesenteric lymph nodes in that part of their function which has to do with infection; next to report the data on the cases of disease of the mesenteric lymph nodes that were found in the records from one hospital from 1914 to Aug. 1, 1936, and third, to point out that a broader interpretation of the mesenteric lymph nodes is definitely indicated regarding their place in diagnosis and treatment.

The fact that 123 unselected cases have been studied and analyzed for comparison may be of interest to other clinicians who appreciate the importance of whatever rôle it is that the mesenteric lymph nodes play in abdominal or in general disease.

Investigators have tried to impress clinicians with the importance of proper and timely treatment of abdominal disease. Practitioners having the responsibility of handling children have been particularly warned not to neglect any case of appendicitis; for indeed, the differential diagnosis of abdominal conditions is often so far reaching and difficult that autopsy alone may determine the nature of a condition that appeared to be relatively mild or easy to diagnose at the time the patient was first seen. This has been pointed out especially in cases in which infection of the upper respiratory tract is present [1] or in cases of a severe exanthem, influenza or scarlet fever.[2]

Furthermore, it appears that enlargement of the mesenteric lymph nodes has been recognized as contributing to the difficulties of diagnosis of abdominal conditions from the time of Hodgkin to the present time.

Mead,[3] of the University of Minnesota, set the example for other workers in successfully determining the anatomic measurements of

1. Brennemann, J.: "The Abdominal Pain of Throat Infections in Children," and Appendicitis, J. A. M. A. **89**:2183-2186 (Dec. 24) 1927.

2. Brandman, H.: Appendicitis and Acute Inflammatory Abdominal Conditions in Scarlet Fever: Reports of Nine Cases and Review of Literature, Arch. Surg. **29**:612-627 (Oct.) 1934.

3. Mead, C. H.: Mesenteric Lymphadenitis Simulating Acute Appendicitis: Quantitative Study of Size of Normal Mesenteric Lymph Nodes, Arch. Surg. **30**: 492-527 (March) 1935.

mesenteric lymph nodes by scientific methods. Although he admitted the possible causes for error, he has given an accurate standard which may be used to obtain an idea of the size and distribution of normal mesenteric lymph nodes. He has shown that the total number of mesenteric nodes varies greatly, from about 30 in a premature stillborn infant to nearly 300 in another full term stillborn infant. The lymph nodes are found in three definite positions, a fact which should be emphasized. The first group of nodes is located at the last anastomosing branching of vessels before the intestine is reached; these are usually the smallest nodes. The second group is found at the next larger anastomosing branches of the large mesenteric vessels, and the third is located at the root of the mesentery where the large vessels arise. As a general rule the largest nodes are those at the root, and they gradually become smaller as the intestine is reached. Mead [3] expressed the belief that there is evidence of an increase in the size of normal mesenteric lymph nodes up to puberty. Accurate understanding of what can be considered normal is most necessary before a surgeon can state that mesenteric lymph nodes are enlarged.

My main interest here has to do with infection or toxemia arising in the intestine and passing to the lymph nodes in the mesentery.

The experiments of Arnold,[4] at the University of Illinois, show interesting data on the functioning mesenteric lymph nodes. Astounding changes were produced in the flora of the intestinal canals of dogs by the mere altering of the hydrogen ion concentration of the intestinal contents, feeding a protein meal or certain other food substances or changing the temperature of the surrounding room. Arnold pointed out this variability of the intestinal flora under the changing conditions just mentioned and stated explicitly his belief that many organisms penetrate the intestinal mucosa only to be destroyed later by the mesenteric lymph nodes and liver, which contain the phagocytes needed for such a function. Heyd [5] recognized the great task of the liver in destroying organisms that are absorbed from the intestinal canal much of the time. The mesenteric lymph nodes as well play a large part in this absorption at all times. Drueck [6] wrote concerning organisms that in all probability are absorbed not only from the ileocecal region but also from the colon and even from the rectum. He associated other foci in the mouth with intestinal disease and increased permeability of the intestines. His evidence appears to be clinical.

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4. Arnold, L.: Bacterial Flora Within the Stomach and Small Intestine: Effect of Experimental Alterations of Acid-Base Balance and of the Age of the Subject, Am. J. M. Sc. **186**:471-480 (Oct.) 1933.

5. Heyd, C. G.: Protective Rôle of the Liver in Abdominal Surgery, Am. J. Obst. & Gynec. **19**:203-210 (Feb.) 1930.

6. Drueck, C. J.: Systemic Infection from Colon, Illinois M. J. **67**:275-279 (March) 1935.

The fact that organisms from somewhere in the body enter the blood stream seems to be related to some of the most interesting of modern experiments—those on periodic infections of the blood stream with pathogenic organisms in otherwise normal persons.[7] More than one instance has been found in which a positive blood culture was obtained for a normal menstruating woman.[8] Other investigators obtained positive cultures from the blood of 173 of 293 otherwise normal, healthy persons.[9] The work of Alvarez [10] as well lends credence to this kind of evidence. Why it is that the pathogenic bacteria found so frequently do not cause manifestations of considerable significance may be explained by the fact that some investigators emphasize the need of a period of sensitization before any infection can become manifest.[11]

A working knowledge of the function of the mesenteric lymph nodes requires an appreciation of the products absorbed from the intestine by the lymphatics. If it is understood that the blood stream carries the finer, more soluble constituents and that the lymphatics can carry many insoluble substances—as is seen from Cuthbert and Ivy's [12] experiment with suspensions of lamp black—by means of the phagocytes which move in their channels, one can understand why many possibilities for contamination are excluded from the blood stream when a foreign substance is placed in contact with its capillaries. Just what molecules or particles can enter the blood and not the lymphatics is not fully known.

If particles as large as yeast cells pass through intestinal mucosa and are found on microscopic examination to be lodged in the liver, as has been reported by Fisher [13] in experiments on animals, there cannot be much doubt that bacteria could flow through the intestinal mucosa into the lymphatics or veins or into both, or into the lymph nodes, where they either are lysed or pass on to the thoracic duct into the general

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7. Cameron, G. C.; Rae, C. A., and Murphy, G. N.: Blood Cultures and Focal Infections: An Experimental Study with One Hundred Healthy Adults, Canad. M. A. J. **25**:131-134 (Aug.) 1931.

8. Kulka, E.: Bacteremia in Normal Menstrual Periods: Case, Zentralbl. f. Gynäk. **54**:171-173 (Jan. 18) 1930.

9. Reith, A. F., and Squier, T. L.: Blood Culture of Apparently Healthy Persons, J. Infect. Dis. **51**:336-343 (Sept.-Oct.) 1932.

10. Alvarez, W. C.: Mesenteric Lymphadenitis in Adults, a Cause of Pseudo-Appendicitis, Indigestion, Diarrhea, and Arthritis, M. Clin. North America **14**:605-617 (Nov.) 1930.

11. Corpaci, A.: Infection: Importance of Specific Sensitization, Soc. internaz. di microbiol., Boll. d. sez. ital. **1**:237 (Nov.) 1929.

12. Cuthbert, F. S., and Ivy, A. C.: Absorption of Carbon Particles from Gastro-Intestinal Tract, Proc. Soc. Exper. Biol. & Med. **32**:1272-1273 (May) 1935.

13. Fisher, V.: Absorption of Yeast from Large Intestine, Proc. Soc. Exper. Biol. & Med. **29**:490-494 (Jan.) 1932.

circulation. The work of Arnold and his collaborators [14] substantiates this idea. Boone and his co-workers [15] stated that the permeability of the intestines is not so marked as the experiments of Arnold would lead him to believe, nor is the absorption of bacteria as rapid in his experiment. He does, however, confirm some of Arnold's findings, especially those concerning the tremendous tide of bacteria that passes through the circulation in anaphylactic shock produced with horse serum.

At this point it is most helpful to note the work of Drinker [16] on the ability of a lymph node to filter out pathogenic organisms experimentally injected into the lymphatic vessels. He concluded from clearcut experimental evidence that a lymph node that is not massaged or compressed will filter out practically all bacteria entering it. If this is taken literally and applied clinically, one finds not only that one has been advising absolute rest in the treatment of peripheral lymphatic infections but also that one may well further consider its application in the treatment of infections of the mesenteric lymph nodes. If from the point of view of mechanics alone it is realized how much increased motion and pressure are caused intra-abdominally by the administration of purgatives which cause straining, one can see how organisms might pass through more than one lymph node by being forcefully pushed on. The same would seem true of any condition, even severe muscular exercise causing increased peristalsis and increased intra-abdominal pressure.

Having taken a broad view of the function of the mesenteric lymph nodes—especially that part having to do with absorption of bacteria, bacterial products and other substances from the gastro-intestinal tract, not to mention the changes resulting from generalized diseases or metabolic disorders—I shall proceed to a brief description of mesenteric lymphadenitis as it is commonly encountered.

DEFINITION

Mesenteric lymphadenitis is the term used to signify inflammation and swelling of the mesenteric lymph nodes, which should be properly considered as a clinical entity, because there is sufficient evidence to prove that this symptom complex is fairly common but can rarely be diagnosed until abdominal exploration. The term has become more than a general term and suggests the definite picture of abdominal disease which has as its apparent sole cause an inflammation of the mesenteric lymph nodes, especially those draining the lower part of the ileum.

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14. Shuger, M., and Arnold, L.: Absorption of Bacteria From Large Intestine, Proc. Soc. Exper. Biol. & Med. **29**:494-496 (Jan.) 1932. Arnold.[4]

15. Boone, T. H.; Chase, E. M., and Brink, H. E.: Intestinal Absorption of B. Prodigiosus, Proc. Soc. Exper. Biol. & Med. **29**:113-116 (Nov.) 1931.

16. Drinker, C. K.; Field, M. E., and Ward, H. K.: The Filtering Capacity of Lymph Nodes, J. Exper. Med. **59**:393-405 (April) 1934.

Unfortunately most investigators agree that the symptoms vary considerably and resemble closely those that lead to abdominal operation for "acute," "chronic," "subacute," "subsiding" or "interval" appendicitis. However, the most popular use of the words "mesenteric adenitis" refers to the more definite picture of the acute type of condition seen commonly in children and young adults.[17] Tuberculosis was at first thought to be the sole cause of this condition and is still believed by some men to be the most probable causative agent.[18] This is questioned by others.[19]

RELATION OF APPENDICITIS AND GENERALIZED DISEASES TO MESENTERIC LYMPH NODES

It is most important to consider any infection of the mesenteric lymph nodes in the light of appendical infection, if for no other reason than because of the frequency of appendicitis, which is an infection that can apparently give rise to lymphadenitis in the mesenteric glands. Appendicitis, however, is not generally found accompanied by gross swelling of the mesenteric lymph nodes. If inflammation of these nodes occurs in all cases of appendicitis, it is not grossly evident at operation and would therefore have to be discovered on microscopic examination. No work has been found which reports a routine sectioning of a mesenteric lymph node at every appendectomy. Statements have been made regarding the scarcity of information about the relationship of acute appendicitis and swellings of the mesenteric lymph nodes. Marchant [20] recorded his impression as long ago as 1900, however, and more modern investigators have emphasized the fact that chronic appendicitis is more likely to be associated with such swellings. The cases described in detail in this article will point out a close relationship.

The opinion as to what constitutes a "normal" appendix probably explains why in many cases mesenteric lymphadenitis has been thought due to something other than appendical infection. A small adhesion to the appendix often seems too insignificant to cause the lymphadenitis found. It is certainly true that adhesions about the appendix must

17. (*a*) Freeman, L.: Obliterating Appendix as Cause of Disturbances Connected with Abdominal Nerves and Lymphatics, Colorado Med. **30**:320-322 (Sept.) 1933. (*b*) Wilensky, A. O.: Mesenteric Lymphadenitis, M. Rec. **98**:770-772 (Nov. 6) 1920.

18. Bell, L. P.: Mesenteric Lymphadenitis Simulating an Acute Abdominal Condition, Surg., Gynec. & Obst. **45**:465-473 (Oct.) 1927.

19. (*a*) Goldberg, S. L., and Nathanson, I. T.: Acute Mesenteric Lymphadenitis: A Clinical Syndrome in Children Simulating Appendicitis, Am. J. Surg. **25**:35-40 (July) 1934. (*b*) Connell, F. G.: Pseudo-Appendicitis, J. A. M. A. **67**: 335-338 (July 29) 1916.

20. Marchant, G.: Adenite dans l'appendicite, Bull. et mém. Soc. de chir. de Paris **26**:77-81, 1900.

indicate previous infection. When routine microscopic examination is not done on apppendixes removed at operation, the presence or absence of signs of inflammation can never be ascertained positively except grossly. When marked adenopathy involving a number of lymph nodes has been found at operation, with a more acute type of inflammation than is found in the appendix, no definite avenue for entrance of the infecting organism has been proved, although the theories have been many, varying from a hematogenous one [19a] to that of the absorption type of transmission through the intestinal mucosa.[21] The adherents to the theory of hematogenous infection of the mesenteric lymph nodes cannot explain the anatomic location of the nodes affected, particularly those of the ileocecal group thought to drain a definite area alone. The believers in local absorption from the intestine which drains into the nodes of the ileocecal group cannot explain fully how this absorption occurs without a demonstrable lesion in or about the intestine or how oftentimes the nodes higher up appear larger than those of the ileocecal group. Then, too, reports of bacterial investigation of appendical infections are not easy to find, though the number of bacteria which have been cultured from appendixes are multiform in examinations reported in detail.[22] Various unusual appendical infections from parasites, such as Oxyuris vermicularis, Endamoeba histolytica and Ascaris, have been described, but no one type of infection has been found associated with mesenteric adenopathy. The difficulty and the possible danger of removing lymph nodes have been mentioned. This is especially true, even though the glands are not calcified in the clinically tuberculous type of swelling and a streptococcus is the cause of the infection.

One of the soundest hypotheses about mesenteric lymphadenitis appears to be based on the general idea of a lymphatic system for the entire body, existing as a unit rather than as separate parts. Macfayden and MacConkey [23] in 1903 called attention to the association of mesenteric lymph nodes, the faucial tonsils and the adenoids as part of the whole lymphoid system. A list of the agents which can cause generalized adenopathy must be understood as including many others besides the following: infections of the upper respiratory tract, exanthems, typhoid, influenza, tuberculosis, syphilis, many cutaneous diseases, poisoning due to certain metals, marked inflammation or ulcers of the intestines, especially those of long duration, actinomycosis, leukemia, sarcoma, Hodgkin's disease, metastatic carcinoma, rickets, scurvy, status lymphaticus and foci of infection of various types, even intestinal stasis.

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21. Carson, H. W.: On the Clinical Aspects of Tuberculous Mesenteric Glands, Lancet **1**:869-872 (June 22) 1918.

22. Gohar, M. A.: The Causal Organisms of Appendicitis, J. Trop. Med. **38**: 146-148 (June 15) 1935.

23. Macfadyen, A., and MacConkey, A.: An Experimental Examination of Mesenteric Glands, Tonsils, and Adenoids, Brit. M. J. **2**:129, 1903.

Recognition of acute mesenteric lymphadenitis as predominating over the inflammation or lack of it in the appendix stimulated many investigators to write about acute mesenteric lymphadenitis as a condition to be differentiated from acute appendicitis and also about the necessity for its proper treatment.[24] Certain reports contain detailed information about the differential diagnosis of abdominal conditions and appendicitis with little or nothing about mesenteric lymphadenitis. No matter, then, what type of infection of the mesenteric lymph nodes is found, it is probably sensible to consider the nodes as being subject to periodic absorption from both the normal and the pathologic gastrointestinal tract. If there is any evidence which proves the presence of associated pathologic changes in the appendix or any other organs, it should be noted.

REPORT OF ONE HUNDRED AND TWENTY-THREE CASES OF DISEASE OF THE MESENTERIC LYMPH NODES

The records of the New York Post-Graduate Medical School and Hospital were consulted in the search for cases of involvement of the mesenteric lymph nodes from any cause between 1914 and Aug. 1, 1936. In the index covering "mesenteric lymphadenitis" it was possible to find recorded 123 cases in which a diagnosis on the chart showed that at some time or other during the patient's stay in the hospital the condition of the mesenteric lymph nodes was pathologic. A search was also made for cases of tuberculosis of the mesenteric lymph nodes, tabes mesenterica, mesenteric lymphadenitis, either acute or chronic, and mesenteric tuberculosis.

There were 8 cases of malignant neoplasm in the group. The only 3 cases in which no other abdominal conditions were recorded except involvement of the mesenteric lymph nodes were those of patients aged 3 months, 10 months and 5 years, respectively. The first, a girl, underwent an exploratory laparotomy, presumably for pyloric stenosis. Nothing but swollen mesenteric glands was found. Recovery was good, but it is significant, perhaps, that appendectomy was done nine years later because of an acute attack of appendicitis. There was nothing on the chart to indicate that a pathologic condition of the glands was found at that time.

The second patient, a boy aged 10 months, died after exploration of the abdomen. Nothing but tabes mesenterica and what appeared to be

24. (*a*) Bergareche: Tuberculous Mesenteric Lymph Nodes: Review of Literature; New Cases, Arch. de med., cir. y especialid. **31**:598-604 (Dec. 21) 1929. (*b*) Strömbeck, J. P.: Mesenteric Lymph-Adenitis: Clinical Study, Acta chir. Scandinav. (supp. 20) **70**:1-254, 1932. (*c*) Wilensky, A. O., and Hahn, L. J.: Mesenteric Lymphadenitis, Ann. Surg. **83**:812-826 (June) 1926. (*d*) Braithwaite, L. R.: Tuberculosis of Glands in Ileocaecal Angle: Cause of Pain in Right Iliac Fossa, Brit. J. Surg. **13**:439-451 (Jan.) 1926. Bell.[18] Wilensky.[17b]

intestinal obstruction were found, the only apparent cause being the involvement of the mesenteric lymph nodes. The appendix was not examined. No postmortem examination was done.

The third patient, a boy aged 5 years, had an operation for what was termed a "tuberculous abscess of the mesenteric gland." The result was good, and the diagnosis was verified by microscopic evidence. The condition of the appendix was not described on the chart.

Two patients were not operated on, although the diagnosis of involvement of the mesenteric lymph nodes was made. One of these was a boy of 2 years, who died of several diseases—diabetes, ulcerative lesions of the colon and ileum and an infection of the upper respiratory tract in addition to mesenteric lymphadenitis. The other patient recovered from symptoms of abdominal disease and an infection of the respiratory tract within a few days without operation.

TABLE 1.—*Distribution of Cases as to Age and Sex*

Age	Number of Cases	Males	Females
Under 1 year	0	0	0
1- 6 (incl. 6)	15	11	4
7-10 (incl. 10)	31	17	14
11-16 (incl. 16)	20	13	7
17-21 (incl. 21)	7	3	4
22-29 (incl. 29)	21	9	12
30-37 (incl. 37)	6	3	3
38-72 (incl. 72)	10	4	6
Total	110	60	50
Under 21	71	42	29
21 and over	39	17	22
16 and under	66	41	25
10 and under	46	28	18

Close analysis of the remaining 110 cases is helpful but must naturally be regarded reservedly, because it is true that these are cases of a most selected type. In many hundreds of other cases in which operation was done for so-called chronic appendicitis, a simultaneous diagnosis of mesenteric lymphadenitis was not made. Free abdominal exploration for swelling of the lymph nodes cannot be carried out in the presence of more acute types of appendicitis. Moreover, surgeons vary in the emphasis they place on such swellings, either while operating or later when dictating the operative findings to the surgical secretary.

With these admissions and with due credit to investigators who have suggested studies like this before, I wish to present the apparently related facts about these 110 cases of mesenteric lymphadenitis, first excluding the 8 in which the condition was associated with an intra-abdominal malignant tumor, 2 in which operation was not performed (the diagnosis in 1 of which is doubtful) and 3 in which there was no condition other than the mesenteric lymphadenopathy, 1 of these being the case of definite tuberculous abscess of a mesenteric gland.

Operation was performed in all cases at the New York Post-Graduate Medical School and Hospital between 1914 and Aug. 1, 1936.

The totals of the average figures and the more interesting facts about the 110 cases, as well as the 5 others, excluding the cases of neoplasm, will show further information (table 2).

The figures in table 2 show that some sort of appendical disease was present at one time or another in 109 of the 115 cases, or 95 per cent. Microscopic proof for this statement was available in 102, or 88 per cent. In 6 others there had been previous operations on the appendix. In another case there was gross, obviously acute appendical involvement. Appendectomy was performed in 104, or 90 per cent, of the total of 115 cases.

Sixty-one of the patients were males and 54 females. The average age was 16.8 years. The youngest patient, a boy 10 months of age, and the eldest, a woman of 72, made the extremes. There were 9 deaths, a mortality of 8 per cent.

TABLE 2.—*Data in 115 Cases of Mesenteric Adenitis*

Average Age	Sex	Died	Acute Appendicitis	Subacute Appendicitis	Chronic Appendicitis	Appendectomy	Other Operations	Evidence of Infection of Upper Respiratory Tract or Marked Focal Infection	Evidence of Disease in Appendix at Any Time	Clinical Mesenteric Tuberculosis
16.8 yr.	61 M 54 F	9 or 8%	13 or 11%	37 or 32%	54 or 47%	104 or 90%	50 or 43%	65 or 57%	109 or 93%	37 or 32%

Complete evidence regarding the mouth as a source of infection is not available for the reason that in 26 cases there were no records of examination of the tonsils and throat. Certainly in 65 cases, or 57 per cent, the existence of some sort of infection of the upper respiratory tract can be proved, or at least the tonsils were present. The fact that the mere presence of tonsils is included may be subject to criticism, but it is done to show in which cases there could have been tangible foci of infection. There were, at most, 22 of the 65 cases in which much obvious infection in the upper respiratory passages was not recorded. That means there were at least 43 cases, or 37 per cent, in which infection of the upper respiratory tract or marked focal infection in the mouth was definitely recorded. There may have been an infection of the upper respiratory tract in another 26 cases, but the records could not be trusted to deny or to affirm such a state.

A consideration of the total figures in the 115 cases of mesenteric lymphadenitis is further amplified by another set of figures for convenience (table 3).

When doubt about the classifying of lymphadenitis was felt, it was overcome by considering the case under the group of chronic infections.

In the group of 115 cases of mesenteric lymphadenitis, there were 74, or 64 per cent, in which the condition was chronic; 8, or 7 per cent, in which it was distinctly acute; 4, or 3 per cent, in which it was purulent, and 37, or 32 per cent, in which it was clinically tuberculous. Some of the cases in the last three groups overlapped in classification, as can be easily seen in the table from the unrelated percentages. The condition in 1 case could not be classified.

The 109 cases, or 95 per cent, with involvement of the appendix at some time or other is an inescapable fact and cannot be overemphasized. The 14 cases, or 12 per cent, in which there was involvement of the gallbladder was probably low for the whole group, because the gallbladder was perhaps not examined as a routine.

TABLE 3.—*Further Data on 115 Cases of Mesenteric Lymphadenitis*

Average Age	Sex	Chronic Mesenteric Lymphadenitis*	Acute Mesenteric Lymphadenitis	Purulent Mesenteric Lymphadenitis	Pronounced Clinical Tuberculosis of Mesenteric Lymph Nodes	Associated Appendicitis at Any Time	Associated Visceroptosis or Constipation	Fecal Material(+) or Fecalith(++) in Appendix	Associated Disease of Gallbladder at Any Time (Proved)
16.8 yr.	61 M 54 F	74 or 64%	8 or 7%	4 or 3%	37 or 32%	109 or 95%	31 or 27%	24+ or 21% 30++ or 26% 54 or 47%	14 or 95%

* These percentages are of the total only and are not completely differentiating or interrelated. For example, sometimes a case is classified as one of chronic lymphadenitis as well as one of clinical tuberculosis of the mesenteric lymph nodes.

The occurrence of visceroptosis or constipation in 31 cases, or 27 per cent, is probably also low for this group, for the reason that such facts are seldom recorded as a routine on the charts when other more evident diseases prevail.

Fecal content in the appendixes, though not always recorded perhaps, seems most significant in 24, or 21 per cent, of the cases. The additional cases, or 26 per cent, in which a fecalith was recorded swell the number to 54, or 47 per cent, in which there was tangible, positive proof of stasis in the appendix, a condition which possibly could have been responsible for a predisposition to the associated mesenteric lymphadenitis as well as to the disease of the appendix so often found.

The main symptoms and abdominal findings for the whole group of 115 cases are presented in table 4.

Indications of the truth about clinical symptomatology can be gained to some extent if the totals presented in table 4 are summed up. They reveal that vomiting occurred and was positively recorded in 58 cases, or 50 per cent of the total. Distention or tympany was recorded in only 6

cases, although they must have been present oftener, as judged by the other acute findings in a few cases. The same is true of peritoneal fluid at operation. Spasm of the abdominal muscles was positively recorded in 41 cases, or 36 per cent, of the total. An abdominal mass was felt in only 11 cases and so recorded in 10 per cent. Rigidity in 18 cases, or 16 per cent, and tenderness in 80, or 69 per cent, were the most common abdominal clinical findings recorded.

Most significant, even without complete evidence, is the fact that recurrent abdominal symptoms were recorded in 92, or 80 per cent, of the total of 115 cases. This does not include any cases in which there was only the one attack of abdominal symptoms for which the patient was admitted to the hospital.

TABLE 4.—*Clinical Symptoms and Abdominal Findings in 115 Cases of Mesenteric Lymphadenitis*

Average Age	Sex	Pre-operative Vomiting	Distention or Tympany	Spasm of Abdominal Muscles	Abdominal Mass	Rigidity	Tenderness	Recurrent Pre-operative Symptoms
16.8 yr.	61 M 54 F	58 or 50%	6 or 5%	41 or 36%	11 or 10%	18 or 16%	80 or 69%	92 or 80%

Average Number of White Blood Cells	Average Maximum Temperature Before Operation	Average Maximum Pulse Rate Before Operation	Average Maximum Temperature After Operation	Average Maximum Pulse Rate After Operation	Other Abdominal Disease*	Tuberculous Mesenteric Lymph Nodes Clinically	Died
11,800	100.2 F.	101 F.	101.6 F.	120	66 or 57%	37 or 32%	9 or 8%

* These include constipation, visceroptosis, disease of the gallbladder, etc., but of course do not include appendicitis or disease of the mesenteric lymph nodes.

The average white blood cell count was 11,800 per cubic millimeter—a significant figure, even without the counts in all cases being included for averages.

The averages for the maximum preoperative temperature and pulse were computed to be 100.2 F. and 101, respectively; postoperatively these averages were 101.6 F. and 120, respectively.

If visceroptosis, spastic sphincter ani, marked constipation and organic intra-abdominal diseases can be included as "other abdominal disease"—either at the time of admission or at other times—then at least 66 cases, or 57 per cent, were thus definitely designated. This figure is exclusive of the appendical involvement in 95 per cent mentioned before as well as of periappendicitis or disease of the mesenteric lymph nodes themselves.

When the condition in 37 cases, or 32 per cent, of such a series was pronounced and recorded as tuberculous mesenteric lymphadenitis, it reveals clearly that tuberculosis still may be causing more mesenteric adenitis than is usually believed. Unfortunately, constancy of laboratory proof for these clinical figures is for all practical purposes lack

ing. Of the 37 cases in which a clinical diagnosis of tuberculous mesenteric lymphadenitis was made, microscopic proof is available for only 4, or 10 per cent. Inoculation of only 1 guinea-pig was recorded, although other tests must have been done, to judge by the operative notes.

TABLE 5.—*Totals in 123 Cases of Disease of the Mesenteric Lymph Nodes*

Cases	Description	Operation	Death	Acute Infection	Chronic Infection	Suppurative Infection	Tuberculous Infection	Unclassified
63	Appendectomy only.....	63	2	4	48	0	11	0
47	Operation in addition to appendectomy and other diseases.....	47	5	3	26	(2)	23	0
3	Nothing recorded but mesenteric adenitis in the abdomen.....	3	1	1	0	(1)	3	0
2	No operation.....	0	1	1	0	(1)	0	1
8	Intra-abdominal malignant growth.....	8	8 (presumably)	1	7	(1)	0	0
123	.....	121 or 98%	17 or 14%	10 or 8%	81 or 66%	(5) or 4%	37 or 32%	1 or 0.8%

TABLE 6.—*Involvement of Appendix in 123 Cases of Disease of the Mesenteric Lymph Nodes, 1914 to Aug. 1, 1936*

Cases	Description	Gross Acute or Chronic Appendical Involvement at Same Time (On Admission)	Appendectomy at Some Time	Previous Appendectomy	Appendectomy Done at Present Admission	Later Appendectomy	Positive Microscopic Evidence of Appendical Involvement Past or Present Admission
63	Appendectomy only....	63	63	0	63	0	62
47	Operations in addition to appendectomy and other diseases.....	41	44	3	41	0	41
3	Nothing recorded but mesenteric adenitis in the abdomen.....	0	1 (9 yr. later)	0	0	1	1
2	No operation.....	0	0	0	0	0	0
8	Intra-abdominal cancer	2	3	1	2	0	3
123	.....	106 or 86%	111 or 90%	4 or 3%	106 or 86%	1 or 0.8%	107 or 87%

To conclude the tabulation of the entire series so as to include all the cases of involvement of the mesenteric lymph nodes from 1914 to Aug. 1, 1936, it is necessary to consider the 8 other cases—besides the 115 so far studied—in which malignant neoplasms were present in the abdomen. Briefly, the cases are divided so as to show the total percentages (table 5).

The data in tables 5 and 6 are self-explanatory and serve to increase the evidence that gives the appendix a major place in the diagnosis and

treatment of abdominal conditions. This cannot be stated without further emphasizing the added fact that of 123 cases of involvement of the mesenteric lymph nodes—the only ones recorded on the charts for thousands of laparotomies in one hospital from 1914 to Aug. 1, 1936—there were 111 cases, or 90 per cent, in which the appendix was sufficiently involved to warrant operation at some time or other. The fact that 8 cases of malignant tumor occurred in this number seems inconclusive, of course, but perhaps interesting for conjecture. The mortality of 100 per cent for the cases of malignant tumor is arbitrary, for there may be a few patients who are alive but cannot be traced or who fall within, as yet, a five year limit of cure.

COMMENT

From this study I believe that the finding in this high proportion of cases of mesenteric lymphadenitis in which the appendix was involved at some time is worth serious consideration, especially since Cave, in a report on a personal series of cases of mesenteric lymphadenitis, found at least 1 in which the appendix appeared normal on gross examination but diseased on microscopic examination.[25] Fortunately the investigation of pathologic reports on the cases herein recorded revealed no appendixes which did not at some time or other show evidence of appendical inflammation. But the fact that a work as frankly surprising as Hosoi's on "normal" appendixes is acceptable [26] makes certain of interest the positive finding of even old appendical disease and might suggest some sort of association, either direct or indirect, with disease of the mesenteric lymph nodes in this study. It seems almost unnecessary to have to emphasize such facts when one stops to realize that mesenteric lymph nodes are made up of lymphatic tissue and that the appendix is, to a large extent also, filled with lymphoid cells. It is my opinion that too much emphasis cannot be put on this point. Benefit from appendectomy is assumed by past evidence,[27] as well as by the infrequency of return of severe symptoms in the cases here reported.

Still another conclusion is suggested by the high percentage of infections of the throat or potential foci of infection in the mouth or throat in this series: Every physician having it in his power to impress on his patients the importance of the removal of foci of infection should do so to the best of his ability. There may be opposition to these measures from those who do not like to advise surgical treatment, especially that

25. Cave, H. W.: Acute Mesenteric Lymphadenitis Simulating Acute Appendicitis, paper read at the meeting of the Surgical Section, New York Academy of Medicine, April 3, 1936.

26. Hosoi, K.: Neurogenic Appendicitis: Study of 195 Cases of Appendicular Neuromas, Am. J. Surg. **22**:428-446 (Dec.) 1933.

27. Wilensky and Hahn.[24c] Wilensky.[17b]

which is elective in the nose and throat, but a moment's consideration will show that such physicians are insufficiently concerned about the patients in the cities where hygiene is at low ebb and where little sunlight, fresh air and decreased outdoor exercise are the rule for the majority.

A large number of investigators, including Andersen,[28] Auguy,[29] Bell,[18] Bonjour,[30] Bose,[31] Braithwaite,[24d] Brown,[32] Cave,[25] Coleman,[33] Corner,[34] du Bourguet and Roquigny,[35] Duteil,[36] Duval and Roux,[37] Felsen, [38] Ferry,[39] Goldberg and Nathanson,[19a] Goldschmidt,[40] Karger,[41] Lamson,[42] Marchant,[20] McFadden,[43] Levin,[44] Lund,[45] Mead,[3] Neuer,[46]

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28. Andersen, K.: Ueber universale mesenteriale Lymphadenitis mit appendixähnlichein Krankheitsbild, Med. rev., Bergen **36**:528-536, 1919; abstr., Zentralbl. f. Chir. **46**:921, 1919.

29. Auguy, J.: De l'adénopathie appendiculaire, Thèse de Lyon, no. 134, 1901.

30. Bonjour, E.: Des adénopathies péri-appendiculaires dans l'appendicite, Thèse de Paris, no. 88, 1901.

31. Bose, M.: Lymphadenitis of Retroperitoneal Glands Simulating Appendicitis, Indian M. Gaz. **69**:579-580 (Oct.) 1934.

32. Brown, H. P.: Acute Mesenteric Adenitis Simulating Appendicitis, S. Clin. North America **9**:1195-1196 (Oct.) 1929.

33. Coleman, E. P.: Acute Mesenteric Lymphadenitis, West. J. Surg. **43**: 193-198 (April) 1935.

34. Corner, E. M.: Tuberculosis of the Mesenteric Glands in Children, Lancet **1**:426, 1912.

35. du Bourguet and Roquigny: Mesenteric Adenopathy Simulating Appendicitis: Three Cases, Soc. de méd. mil. franç., Bull. mens. **28**:72-75 (April) 1934.

36. Duteil, P. H.: Des adénites péri-appendiculaires et mésentériques en rapport avec l'appendicite, Thèse de Bordeaux, no. 99, 1914.

37. Duval, P., and Roux, J. C.: Temporary Compression of Duodenum Due to Mesenteric Adenopathy Caused by Appendicular Infection: Case, Bull. et mém. Soc. nat. de chir. **60**:1239-1243 (Dec. 1) 1934.

38. Felsen, J.: Appendicular Form of Bacillary Dysentery, with Notes on Mesenteric Adenitis and Inflammation of Distal Portion of Ileum, Am. J. Dis. Child. **50**:661-672 (Sept.) 1935.

39. Ferry, A.: Etude clinique sur les adénopathies péri-appendiculaires, Thèse de Paris, no. 52, 1900.

40. Goldschmidt, W.: Mesenteric and Retroperitoneal Suppuration in Differential Diagnosis of Appendicitis, Wien. klin. Wchnschr. **33**:1416 (Jan. 1) 1920.

41. Karger, P.: Symptomatology of Abdominal Pains: Value in Diagnosis of Disorders of Mesenteric Lymph Nodes, Jahrb. f. Kinderh. **139**:91-96, 1933.

42. Lamson, O. F.: Mesenteric Lymphadenitis and Acute Appendicitis, S. Clin. North America **11**:1061-1063 (Oct.) 1931.

43. McFadden, C. D. F.: Mesenteric Lymphadenitis and Its Clinical Manifestations, with Special Reference to Its Differential Diagnosis from Appendicitis, Brit. M. J. **2**:1174-1177 (Dec. 24) 1927.

44. Levin, O. A.: Mesenteriolitis and Its Significance for Symptomatology, Diagnosis and Clinical Aspects of Appendicitis and Its Complications: Histology and Clinical Studies, Beitr. z. klin. Chir. **160**:491-521, 1934.

(Footnotes continued on next page)

Parker,[47] Pozzi,[48] Prado and Montenegro,[49] Premoli,[50] Pribram,[51] Quénu,[52] Segar and Rosenak,[53] Short,[54] Speese and Klein,[55] Struthers,[56] Wagner [57] and Wilensky,[17b] have stressed the similarity of the symptoms of mesenteric lymphadenitis to those of appendicitis. Certain others of these recognized the simultaneous occurrence of chronic appendicitis and mesenteric adenitis, notably Marchant, Pozzi, Premoli and Speese and Klein. It is well known that mesenteric adenitis can follow appendicitis, and instances are reported by Duval and Roux,[37] Ricard and Michaux [58] and Zapel.[59] Acute appendicitis occurs in association with mesenteric lymphadenitis less frequently than with chronic appendicitis. Almost all writers on the subject admit that this is true. Some, including Pozzi, believe that the appendical infection may follow the lymphadenitis.[47] This problem appears to be as yet unsolved, as previously suggested.

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45. Lund, F. B.: Tuberculosis of the Mesentric Glands Simulating Appendicitis, Boston M. & S. J. **167**:918-921, 1912.

46. Neuer, H.: Tuberculosis of Mesenteric Lymph Nodes and Its Complications (Acute Appendicitis and Compression of Choledochus), Beitr. z. Klin. d. Tuberk. **80**:523-531, 1932.

47. Parker, D. W.: Tuberculous Mesenteric Glands Simulating Appendicitis, Boston M. & S. J. **167**:915-918, 1912.

48. Pozzi, G.: Syndrome of Chronic Appendicitis as Complication of Adenomesenteritis, Arch. ed atti d. Soc. ital. di chir. **38**:635-637, 1932.

49. de Almeida Prado, A., and Montenegro, J.: Mesentery Tuberculosis, Chronic Appendicitis and Meso-Sigmoiditis of Tuberculous Origin: Case, Rev. sud.-am. de méd. et de chir. **2**:21-44 (Jan.) 1931.

50. Premoli, F.: Calcification of Lymph Nodes; Chronic Appendicitis Associated with Calcified Mesenteric Lymph Nodes Resembling Renal Calculi; Case, Rev. méd. del Rosario **21**:113-117 (March) 1931.

51. Pribram, B. O.: Umbilical Colic, Lymphangitic Form of Appendicitis and Mesenteric Lymphangitis, München. med. Wchnschr. **82**:942-944 (June 14) 1935.

52. Quénu, M.: De l'adénopathie mésenterique dans les appendicites aiguës toxi-infectieuses, Bull. et mém. Soc. de chir. de Paris **28**:540-549, 1902.

53. Segar, L. H., and Rosenak, B. D.: Non-Tuberculous Mesenteric Lymphadenitis in Childhood, Am. J. Digest. Dis. & Nutrition **2**:356-360 (Aug.) 1935.

54. Short, A. R.: Symptoms Due to Mesenteric Lymphadenitis, Lancet **2**:909-912 (Nov. 3) 1928.

55. Speese, J., and Klein, T.: Acute Mesenteric Lymphadenitis, Associated with Chronic Appendicitis, S. Clin. North America **4**:261-263 (Feb.) 1924.

56. Struthers, J. W.: Mesenteric Lymphadenitis Simulating Appendicitis, Edinburgh M. J. **27**:22-26 (July) 1921.

57. Wagner, J.: Acute Mesenteric Lymphadenitis Following Trauma and Simulating Acute Appendicitis, Internat. J. Surg. **38**:113-114, 1925.

58. Ricard, in discussion on Abcès du foie d'origine appendiculaire, Bull. et mém. Soc. de chir. de Paris **26**:68, 1900. Michaux, in discussion on Abcès du foie d'origine appendiculaire, ibid. **26**:69, 1900.

59. Zapel, E.: Mésenteriolitis Appendicularis and Post-Appendicitic Changes in Venolymphatic System of Mesenteriolum, Arch. f. klin. Chir. **169**:180-192, 1932.

The various possible complications of mesenteric lymphadenitis need only to be mentioned to impress the reader with the great significance they may assume in the disease: obstruction of the common duct, duodenal obstruction, arrosion of the mesenteric artery with resulting hemorrhage, thrombosis of the mesenteric vessels, mesenteric pyemia and suppuration, intestinal obstruction, rupture causing general peritonitis or tuberculosis peritonitis, the formation of a fistula; loose bodies in the peritoneal cavity, compression of ureters, hernia from possible overstraining when pain or partial obstruction is present, miliary tuberculosis, abscess of the psoas muscle or abscess pointing through Petit's triangle, abscess of the liver, subdiaphragmatic abscess and cholecystitis and chronic hepatitis.

Should there not be, then, a greater interest in the mesenteric lymph nodes, and can there not be and should there not be a routine recording of their condition, not only at postmortem examination, but also on the living person at every laparotomy?

Since both Alvarez and Heyd emphasize the importance of the work of Adami, who stressed autointoxication and subinfection from the bowel twenty-two years ago, there must be a reason for their not discarding this belief.[60] Just why it is that in certain cases visceroptosis, constipation and stasis are accompanied by mesenteric lymphangitis is not known.[61] Why these conditions could allow, predispose to or possibly incite mesenteric adenopathy is not known. Nor is it known what stimulates the onset of Hodgkin's disease or leukemia, unless it is a virus or activation from some infective process of the upper respiratory tract. Perhaps the relation of the nervous system to chronic appendicitis should be thought paramount to any other predisposing causes, when one considers that Kobro attributed chronic appendicitis to a disturbance of the sympathetic nervous system.[62] Again, Hosoi's finding of neuromas in 82 per cent of obliterated appendixes seems interesting if not pertinent in this connection.[26]

Here a most interesting fact may aid in a partial solution of this problem. Bezecny[63] in 1933 reported the finding of a histamine-like

60. (*a*) Heyd, C. G.; MacNeal, W. J., and Killian, J. A.: Hepatitis in Its Relation to Inflammatory Disease of the Abdomen: A Clinical and Laboratory Study, Am. J. Obst. & Gynec. **7**:413-430 (April) 1924. (*b*) Heyd, C. G.: The Liver and Gall-Bladder Disease, New York State J. Med. **36**:974-978 (July 1) 1936. (*c*) Alvarez.[10] (*d*) Heyd.[5]

61. Brian, P.: Les adénopathies mesenteriques et la stase intestinale, Thèse de Paris, 1925. Connell.[19b]

62. Kobro, M.: So-Called Primary Chronic Appendicitis as Manifestation of Disturbance of Sympathetic Nervous System, Norsk mag. f. lægevidensk. **94**:856-886 (Aug.) 1933.

63. Bezecny, R.: Histamin und Lymphgefäss, Arch. f. Dermat. u. Syph. **167**: 386-393 (Jan. 20) 1933.

substance in lymph vessels which can cause a type of inflammation comparable to lymphangitis. One step further makes it possible that an adenitis might be caused in the same way. If so, the etiology of mesenteric lymphangitis may be clear.

If the normal liver deaminizes all the nitrogenous metabolites which enter it constantly in the form of toxic amines from the portal system, there is a chance that a subnormal liver—from overwork or subinfection—in persons who have sedentary living habits, who suffer from constipation and visceroptosis and who overeat, might allow such an accumulation of poisons resembling histamine as could cause chronic changes in the mesenteric lymph nodes, with their resulting flare-ups into a disease syndrome at the time of definite points of saturation or added transient bacterial insult, whether pyogenic or tuberculous. This necessarily would require that the lymphatic endothelium should become permeable to the amines normally carried to the liver by the portal veins. So far as I know, there is nothing to controvert this hypothesis. The great power of the liver to recuperate would explain the variability of changes and the inconstancy of finding gross abnormality of the liver and would lend credence to the still incomplete explanation for the location of the affected mesenteric lymph nodes, because there would be a tendency for the lymphatics to drain higher toward the root of the mesentery, as is usually the case even when the ileocecal glands are particularly prominent. This would not be expected from localized ileocecal lesions and truly enough is seldom seen. The finding of associated disease of the gallbladder in 14 of the cases in the series reported herein falls in line directly with the facts just mentioned and appears to bear out Heyd's ideas concerning hepatic function, hepatitis from chronic subinfection in the gastro-intestinal tract, visceroptosis and constipation.[60b] If the average age of the patients in this series of cases were greater, I believe most emphatically that there would be a correspondingly higher ratio of hepatic disease.

DIAGNOSIS

Explanation of certain data summarized from the series of cases reported on here for diagnostic purposes will be expressed simply, in order, if possible, to present a few constructive suggestions.

Generally speaking, the various forms of mesenteric lymphadenitis conform to symptoms which directly bear out their findings at operation or postmortem examination. There may be acute symptoms, a marked rise in the number of leukocytes, a high temperature and rapid pulse and every evidence of severe intra-abdominal abnormality or infection, such as might be expected from acute appendicitis. On the other hand, an average normal person may present himself with nothing more than a sticking pain in the right side and with perhaps no greater complaint

than constipation. The temperature, the pulse rate, and the leukocyte count may all be normal or practically so. The question is to try to decide on a diagnosis, if possible, regardless of editorials and original contributions which mention that it is difficult. In one group of the 123 cases analyzed—the 63 in which simple appendectomy alone was performed—there were 4 cases, or 6 per cent, in which the diagnosis of mesenteric lymphadenitis was made preoperatively. In the group of 47 there were possibly 2 cases, or 4 per cent, in which the diagnosis was made before operation. That makes about 5 per cent of the 123 unselected cases in which the correct diagnosis was made preoperatively.

Regardless of the fact that operation will reveal the diseased glands, one should try to diagnose the condition preoperatively to the best of one's ability. Obviously the most important suggestions for better diagnosis are a complete history and physical examination. By a complete history is meant one that is obtained by a clearly defined plan of interrogating the patient, or family when necessary, for positive and not for negative facts. The particular points to look for are family background, especially for tuberculosis, dysentery and parasitic, exanthematous, syphilitic and metabolic diseases, and next, for a past history of tonsillitis, sore throat, exanthems, severe sinus infections or carious teeth, disease of the middle ear, food poisoning, typhoid, dysentery and the taking of cathartics. Occupation, habits and marital history may offer considerable enlightenment, if there is evidence of repeated miscarriages, sterility and abnormal children. The amount of exercise at the time the patient is seen compared with what was habitual previously might offer an aid to the diagnosis of gastro-intestinal stasis. The same might be said of increased weight, overeating and other such suggestive findings.

In the entire series of cases, including those of intra-abdominal malignant neoplasm, recurrent symptoms were positively recorded before those complained of on admission in 92 cases, or 80 per cent. Again one should remember the number of cases in the total series of 123 in which there was evidence of disease of the appendix at some time or other, namely, 111 cases, or 90 per cent. Why, then, should these recurrent symptoms be attributed entirely to the mesenteric lymph nodes?

One should keep in mind recurrent symptoms, foci of disease in the upper respiratory tract, constipation, visceroptosis and acute and chronic appendicitis with associated mesenteric lymphadenitis and perhaps in the future the diagnosis of mesenteric lymphadenitis can often be made preoperatively. It goes without saying that the absolute diagnosis of visceroptosis in, commonly, a thin, psthenic adolescent of sedentary, unhealthy habits must be left to the roentgenologist. The presumptive diagnosis is usually simple to make. Constipation should not be diagnosed without the explanation to the patient first that by constipation is

meant the difficult passage of a hard stool, not necessarily a stool every other day or at irregular times.

In continuing with the history, it is most important to get a good description of the type of pain experienced in the abdomen. In all but possibly 2 cases in this series, excluding the cases of cancer, there was abdominal pain. Why it is that accurate words to describe pain are not used oftener is hard to say. It is my belief that the doctor is responsible for not explaining to the patient the finer shades of meaning he is trying to elicit rather than merely the word pain, undifferentiated. Was it a generalized pain at first or a sticking, sharp, sickening pain in the region of the right lower abdominal quadrant? Thus should the questions be qualified, reapplied and rechecked till a reasonable sequence in answer is obtained. Some writers stress the sudden sticking pain, the variable vomiting, the duration of pain of only a few minutes and the freedom from pain between attacks.[24d] The right lower quadrant is commonly the seat of the pain. Tenderness is noted by the patients also. Here again it is fair to state that suggestion may play a part, but not to the extent that many unsuspected relative truths will not be elicited, in contrast to what is discovered from a hastily written history or scant examination. The best understanding in any case is gained by a meticulous physical examination.

Physical examination should not be thought of just in terms of a routine examination of the throat, heart, lungs and abdomen; rather one should bear in mind that the patient is in the precarious position of facing an abdominal operation. When a pediatrician examines a baby in proper fashion he carries around all the needed instruments to include good visualization of the throat and the nose and ears as well. When a surgeon or an embryosurgeon examines a patient sent into the hospital with a diagnosis of chronic appendicitis or some other diagnosis, he knows he has to do a urinalysis, obtain blood counts and examine the chest. When this is all that he does, the proper diagnosis of disease of the mesenteric lymph nodes cannot be made preoperatively. There must be a careful examination of the nose, throat, eyes and ears. Roentgenograms must be made of the teeth, and a method of habitually palpating the cervical lymph nodes must be appreciated as diagnostically valuable.

The continuance of the examination further than already described should include not only examination of the heart and lungs but also of the abdomen. Palpation of all the lymph nodes in the body near enough to the surface to be felt should be particularly emphasized.

To sum up, the abdominal signs are variable—more so than is to be expected in the more typical cases of acute appendicitis. In other words, if everything points toward appendicitis as it is usually thought of, when abdominal signs are not typical—that is, some are lacking in the face

of a typical history of appendicitis—one should think of a diagnosis of mesenteric lymphadenitis. If, in addition to normally expected signs of acute appendicitis, a spastic sphincter ani or visceroptosis is obvious, or a hard stool is palpable, one should again think of a diagnosis of mesenteric lymphadenitis. This does not mean that appendicitis should necessarily be omitted from simultaneous consideration or that the operation should be postponed. No diagnosis is intended to be recommended which causes delay and resulting morbidity from neglected appendicitis.

If there are any positive signs of disease of the gallbladder or gallstones, tenderness in the region of the liver, with a history of indigestion, gas and other typical manifestations, in addition to the symptoms lower in the abdomen, and a diagnosis of appendicitis or mesenteric lymphadenitis is being considered, these two conditions should not be omitted from the preoperative diagnosis or impression because of the predominance of symptoms in the upper part of the abdomen.

Laboratory findings, when positive, are of great help in pointing to mesenteric lymphadenitis. No one positive laboratory test is absolute, however, although in skilled hands a roentgenogram may often show calcified abdominal lymph nodes, especially if roentgenograms are made as a routine. This finding applies to the tuberculous type of mesenteric lymphadenitis in most cases anyway.

Further, tests for Ascaris, Oxyuris vermicularis and Endamoeba histolytica are indicated whenever possible, but even when these organisms are found they do not constitute a uniform proof of mesenteric lymphadenitis. Lewis and others have stated that since undulant fever is now known to be associated at times with mesenteric lymphadenitis, in cases in which it is suspected by the symptoms and the fever curve, agglutination tests for the organisms of the melitensis group are recommended.[64] The Widal test, cultures of material from the throat, nose and teeth and the Wasserman and Kahn tests all have a place in diagnosis which should not be minimized.

One of the most interesting tests on which all kinds of opinions can be obtained is the tuberculin test. I hesitate to enter on a discussion of it, but for the sake of possible help a few hints are given. There are various tuberculin tests which can be used. The Mantoux test is well recognized and probably gives as good results as any. A positive reaction to this test has little significance, however, in any but the youngest children—arbitrarily, say, aged 5 or under. Even then it may not indicate a tuberculous infection unless the infection is the first one or the test is done a certain time after the onset of the first infection. A negative reaction, however, which is repeated in a day or two in a person

64. Baumgarten, E. C.: Surgical Significance of Acute Glandular Fever, J. Michigan M. Soc. **24**:243-245 (May) 1925.

with an illness such as, for example, acute mesenteric lymphadenitis may mean that the infection is tuberculous, especially if a few weeks later the reaction to the test is positive (without any other intervening illness). After the age of 5 years a positive reaction to the tuberculin test is so common as probably to be worthless for diagnosis in most cases. In the series of cases reported on here this test did not offer much help. However, this should not keep it from being used in suitable questionable cases for interpretation by those qualified to judge its significance. It is not a test to be used by any one unaccustomed to its broadest, common sense application.

Although nothing definite can be suggested of diagnostic importance from the temperatures and pulse rates in the present series of cases, they can be referred to for averages as well as for extremes. The hope is expressed that clinicians will notice the similarity of these figures to those in all cases of appendicitis except the most acute type. Without wishing to seem too repetitious, I think that this strengthens my belief that appendicitis should not necessarily be distinguished from mesenteric lymphadenitis but should be considered with it. Nothing particular is of aid here in differentiating appendicitis by temperature, pulse or white cell counts.

Negative results of urinalysis may aid in diagnosis, but the presence of blood can mean pressure on the ureter from mesenteric lymph nodes and should be remembered.

Without seeming to make too sweeping a statement, it is possible to suggest further that complications of the frankly severe tuberculosis of the mesenteric lymph nodes must naturally cloud the picture and therefore can often be diagnosed only at operation. The same is true of complications of appendicitis, or malignant tumors, of course. Roentgenograms are of help to show congenital defects as well as stasis, reflex gastric or duodenal spasm, poor emptying of the appendix, colonic spasm, diverticulosis or Lane's kink.

There is, so far as I know, unfortunately little else that can be done preoperatively to aid in diagnosis. Even in a large percentage of cases some of the suggestions must be postponed, because of lack of time, until postoperative convalescence has begun if the exact etiology is to be explicitly determined before the patient is discharged.

I wish to offer the suggestion that repeated blood cultures, even in the absence of sepsis of a high grade, should be taken to try to attain in the future some uniformity of findings in a large group of these patients. The only positive blood culture in this series was obtained in a case of terminal ileitis and peritonitis.

If other suggestions have been omitted it is because so much has been written by others on the subject.

TREATMENT

The treatment of mesenteric lymphadenitis must depend entirely on the general attitude the surgeon takes toward infections of the lymph nodes and on the degree of inflammation found.

It is my belief that the three factors of (1) infection from the gastro-intestinal tract, (2) absorption of histamine-like products of decomposition from the intestines and (3) damaged hepatic function may lead to mesenteric lymphadenitis. The treatment depends on which of these factors appears to be the exciting cause or the most outstanding predisposing element.

The operative treatment needs little explanation further than that suggested by numerous others except that the disease should be recognized and classified definitely at operation and that appendectomy be immediately performed. Preoperative diagnosis is rare, so that the diagnosis at operation is often a surprise. The raising of the ileum into the wound so as to expose the intestine to the air is advised for the purpose perhaps of changing the oxygen tension of the intestinal wall. This has helped in tuberculous peritonitis and other tuberculous abdominal conditions. It seems to help whether tuberculosis is diagnosed or not and should be done until a hyperemia appears in the wall of the intestine. The treatment of frankly caseous lymph nodes needs no description beyond that given in many other articles. The spreading infection through the abdominal cavity from ruptured mesenteric lymph nodes should be treated according to conservative surgical principles. If the process does not appear localized or it seems that evacuation of profuse purulent material is needed, drainage should be done. If a drier, localized, caseous mass seems operable, one should not operate to remove it in its entirety without realizing that an extensive resection of small intestine may be necessary before the operation is completed, because the mesenteric vessels are so intimately and firmly adherent to such masses. It is possible, at times, to remove certain offending mesenteric lymph nodes without embarrassing the intestinal circulation. If resection of any part of the intestine seems inevitable in the cases of serious involvement that may or may not be tuberculous, it is best to do an entero-enterostomy immediately and close the wound without drainage. There is seldom need for these procedures in any but frankly tuberculous involvement.

In almost all cases no further procedure other than appendectomy without drainage is necessary unless the condition of the appendix indicates that drainage would be safer. Biopsy of the glands is needed largely for an addition to knowledge and seldom for therapeusis. It is dangerous when there is even slight likelihood of a streptococcic infection being present.

A careful routine postoperative search for the cause of the swollen mesenteric lymph nodes is suggested as a most sane prophylactic assurance of better health in the future. A search for the causes of the symptoms which were suggested as preoperative aids to diagnosis should be carried out postoperatively if no time was available for this before.

In general, then, one should make sure that all foci of infection are removed, that the diet is proper for the individual patient, that exercise, exposure to sunlight, rest and regular intake of fluids are started and that removal of all predisposing causes of visceroptosis, constipation, disease of the gallbladder or liver, anemia and nervous disorders is effected simultaneously postoperatively after a routine simple appendectomy or such operation as appeared to be indicated, in addition to appendectomy. The fact that such uniformly good results have been obtained by this operative procedure again appears to be evidence for the belief that there is some sort of association between the appendix and the mesenteric lymph nodes.

CONCLUSIONS

It is not possible to conclude definitely that mesenteric lymphadenitis is an entity completely separate from appendicitis or many other intra-abdominal conditions.

There is evidence to indicate that mesenteric lymphadenitis either has been occurring more commonly or that members of the surgical staff have been more on the lookout for it during the past few years.

In a period from 1914 to Aug. 1, 1936, during which appendicitis was diagnosed in 16,964 cases in all services of the New York Post-Graduate Medical School and Hospital, there were found only 123 cases of all forms of disease of the mesenteric lymph nodes clearly recorded on the charts.

A close study of these cases in the face of admitted omissions on some charts reveals most interesting and, I believe, high percentages of conditions associated with mesenteric lymphadenitis.

In approximately 90 per cent of the cases in this series appendectomy was performed at one time or another. Proof of this definite appendical infection was positive in approximately 87 per cent by microscopic evidence alone.

The incidence of foci of infection in the upper repiratory tract is sufficiently well recorded to warn examiners when thinking of a diagnosis of mesenteric lymphadenitis to be especially on the lookout for evidence of it either in the patient's history or during the examination.

A clinical diagnosis of tuberculous mesenteric lymphadenitis was made in 32 per cent of the 123 cases but was not substantiated by microscopic evidence or other proof except in a few cases.

Associated conditions which were particularly noteworthy included visceroptosis, constipation and disease of the gallbladder and in 8 cases intra-abdominal malignant tumor.

The history of recurrent symptoms is so common in this series that it probably deserves a place among the marked points favoring a diagnosis of mesenteric lymphadenitis.

Although conclusions may be somewhat speculative, I believe that benefit can be gained from the detailed analyses of 123 cases herein reported with regard to clinical symptoms, findings, diagnosis and mortality.

Among the cases of mesenteric lymphadenitis in which there was little beyond involvement of the appendix, there were several in which the appendix contained fecal material or a fecalith and at times the Oxyuris vermicularis.

It is probably not an altogether safe procedure to remove a mesenteric lymph node.

Appendectomy or any other procedure necessary to remove abnormalities which may have had something to do with the occurrence of mesenteric lymphadenitis is the prescribed treatment.

From clinical and experimental reports in the literature, it seems probable that the tremendous importance of the mesenteric lymph nodes has been underestimated in the role that they play in infections of the gastro-intestinal tract and in generalized diseases.

The suggestion appears fitting that intestinal stasis and the conditions contributing to it allow chronic absorption of histamine-like substances which can cause mesenteric lymphadenitis, especially when the appendix is abnormal. Bacterial sensitivity in the gastro-intestinal tract is probably not sufficiently appreciated, may possibly be caused in part by the appendix and may offer a new line of approach toward future immunization and therapy.

SUMMARY

An attempt is made to focus attention on the importance of the function of the mesenteric lymph nodes in absorbing infection from the intestinal tract.

Of the 123 cases of disease of the mesenteric lymph nodes found in a twenty-two year period, an increasing number is noted in which a diagnosis of mesenteric lymphadenitis was made, especially during the past few years. The diagnoses in the 115 cases particularly studied were made by sixteen surgeons on the same staff. Important clinical features, symptoms, findings and mortality figures are given in detail in the different tables, with a discussion of each table immediately following its presentation.

Diagnosis is briefly touched on to emphasize, if possible, in a general way what is needed to increase the number of cases in which mesen-

teric lymphadenitis is diagnosed preoperatively. There is necessarily no need to dissociate it from appendicitis. This importance of complete history and thorough physical and laboratory examinations, not only before but after operation, is stressed, if any diagnosis is to be positive in these cases.

Treatment is also briefly outlined with the idea of emphasizing nothing that has not in all probability been advised before by other writers on the subject, possibly in greater detail.

A summary and conclusions complete this communication.

Dr. Charles Gordon Heyd started me on this study, and Dr. Thomas H. Russell, Director of Surgery at the New York Post-Graduate Medical School and Hospital, made its continuation and the presentation of this communication possible.

PRODUCTION OF OSTEOSARCOMA IN A MOUSE BY THE INTRAMEDULLARY INJECTION OF 1, 2-BENZPYRENE

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AND
A. D. BISSELL, M.D.
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Primary malignant neoplasms of bone have been produced experimentally by irradiation. Schürch [1] induced an osteosarcoma in the mandible of a rabbit by the application of a radium needle directly to the cortical surface. Lüdin [2] produced a chondrosarcoma in the tibia of a rabbit by repeated exposures to the roentgen rays (total dose, 8,000 roentgens). Schürch and Uehlinger [1] produced three ossifying sarcomas of the femur in rabbits by intra-osseous injections of minute quantities of radium salts. Widespread ossifying metastases in the lungs, spleen, liver and lymph nodes were observed. In two other animals nonossifying fibrosarcomas of bone developed. Daels [3] and Sabin, Doan and Forkner [4] also produced fibrosarcoma of bone in animals by means of radioactive substances.

In Martland's [5] series of patients who were poisoned by the prolonged ingestion of radioactive material, which accumulated in the skeleton, nonossifying fibrosarcomas of bone developed. These instances constitute experiments in man comparable to the experiments in animals just cited.

Apparently little work has been done on the possible effects of carcinogenic chemicals on the skeletal system. Woglom [6] and Seelig and

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This work was facilitated by a grant from the Cancer Research Institute of the Chicago Womans' Club.

From the Department of Surgery and Division of Roentgenology of the Department of Medicine, University of Chicago.

1. Schürch, O., and Uehlinger, E.: Arch. f. klin. Chir. **183**:704, 1935.

2. Lüdin, M.: Acta radiol. **15**:553, 1934.

3. Daels, F., and Bacten, G.: Bull. Assoc. franç. p. l'étude du cancer **15**:162, 1926; **20**:32, 1927; Lancet **2**:666 (Sept. 25) 1926.

4. Sabin, F.; Doan, C., and Forkner, C. E.: J. Exper. Med. **56**:267, 1932.

5. Martland, H. S., and Humphries, R. E.: Osteogenic Sarcoma in Dial Painters Using Luminous Paint, Arch. Path. **7**:406 (March) 1929.

6. Woglom, W. H.: Experimental Tar Cancer, Arch. Path. **2**:533 (Oct.) 1926.

Cooper,[7] in a review of the literature on tar cancer up to 1931, based on over 600 reports, do not mention observations on the application of tar directly to bone. Bernard[8] injected tar into the medullary cavities of the femurs of rats and observed an "erythroleukemic syndrome," but no changes in the bone are reported. Steiner[9] implanted pellets of tar containing 1 mg. of 1, 2, 5, 6-dibenzanthracene into the femurs of rats and guinea pigs but observed no tumors after one year. Ilfeld[10] inserted pellets of cholesterol containing 1, 2-benzpyrene into the medullary cavities of the femurs of eleven rats but observed no tumors after one year.

Dunning, Curtis and Bullock[11] in over 700 tumors in mice and rats produced by the subcutaneous injections of benzpyrene and of dibenzanthracene in liquid petrolatum observed two osteoid sarcomas, i. e., sarcomas containing bone and cartilage. The latter are to be regarded as instances of metaplasia in sarcomas of the soft parts and are analogous to the few instances of ossification that have been observed in such sarcomas in man or to the few cases of true osteosarcomas that have been observed to arise extraskeletally.

EXPERIMENTAL WORK

The purpose of the experiments recorded here was to observe the effects of carcinogenic chemicals on bone by intramedullary injections.

Experiment 1.—Adult white rats were used, and 8 mg. of 1,2,5,6-dibenzanthracene dissolved in 0.5 cc. of lard was injected into the medullary cavity of the left femur by acute flexion of the knee and the insertion of the needle through the skin and inferior articular surface (intracondylar region).

Such an injection produces acute fat embolism, and if not carried out slowly causes immediate death of the animal.

Twenty rats surviving the injections lived for from six to twelve months. No tumors were produced.

Experiment 2.—A procedure similar to that described in experiment 1 was followed, except that 8 mg. of 1,2-benzpyrene dissolved in 0.5 cc. of liquid petrolatum was employed, and injections were made not only into the medullary cavity of the femur but also into the cortical surface. Five rats survived, and of these, three presented fascial spindle cell sarcomas of the thigh by the end of the sixth month; tumor had not developed in the remaining two by the end of the tenth month.

Experiment 3.—In twenty-four white mice 6 months of age or older, the genetic history of which was unknown, a longitudinal incision was made over the left

7. Seelig, M. G., and Cooper, Z. K.: Am. J. Cancer **17**:589, 1933.

8. Bernard, J.: Am. J. Cancer **22**:131, 1934.

9. Steiner, P.: Personal communication to the authors.

10. Ilfeld, F. W.: Am. J. Cancer **26**:743, 1936.

11. Dunning, W. F.; Curtis, M. R., and Bullock, F. D.: Am. J. Cancer **28**:681, 1936.

knee joint, and the inferior articular surface of the femur was exposed. A sharp probe was inserted upward into the shaft, and crystals of 1,2-benzpyrene were pressed into the medullary cavity through these holes. Some of the crystals adhered to the surrounding muscles. The wounds were closed by interrupted silk sutures. Of eight of this group that survived from four to six months, spindle cell sarcomas developed in four in the lower part of the thigh surrounding the shaft of the femur. The latter was not extensively eroded. The tumors did not arise primarily in the bone but were sarcomas of the soft tissue.

In the remaining twelve animals a similar procedure was carried out, except that small cylinders of cholesterol from 4 to 5 mm. long and 1 mm. or less in diameter and containing 1,2-benzpyrene (10 per cent by weight) were inserted into the medullary cavity of the femur. In one instance the shaft of the femur was split by insertion of the probe, and in addition to placing a cylinder of cholesterol in the fractured shaft the probe was inserted into the tibial shaft through the upper articular surface; small fragments of cholesterol and benz-

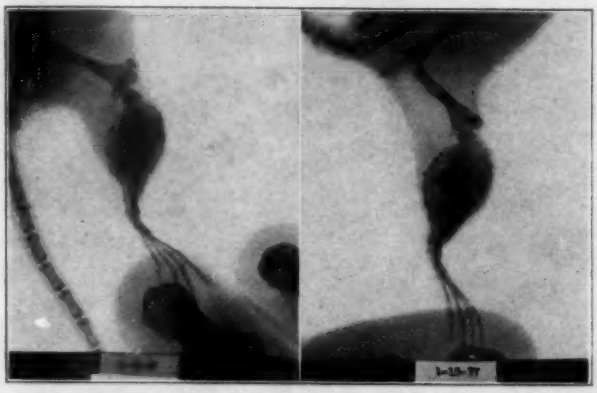

Fig. 1.—Roentgenograms of an osteosarcoma in the tibia of a mouse induced by intramedullary implantation of a mixture of 10 per cent benzpyrene and cholesterol. There was increased new bone formation in the tumor during the twelve day interval between roentgenographic examinations.

pyrene were rammed downward into the tibia. Three animals of this group survived from eight to nine months. Sarcoma did not develop in two. A hard fusiform swelling developed in the tibia of the animal which had also received a tibial implant; the swelling was more pronounced about the upper portion where the concentration of benzpyrene was greatest. Roentgenograms (fig. 1) showed irregular mottling due to new bone formation in the swelling about the tibia. The appearance was characteristic of a primary osteosarcoma. During the subsequent three weeks the swelling increased in size, and another series of roentgenograms showed considerable increase in the amount of new tumor bone. The lungs appeared clear. By this time the animal suddenly became ill and apathetic, and respirations were labored. Because transplantation of the tumor was to be carried out, the animal was then killed, although it was planned to

preserve the animal as long as possible to permit the development of ossifying metastases.

Gross examination of the tibial tumor showed it to be coarsely lobulated, gray and very firm. The surrounding muscles were pushed outward, but their deeper aspects appear to have been invaded by the tumor. Examination of the left femur showed the cylinder of benzpyrene and cholesterol in place; there was no evidence of neoplasm.

When the abdomen was opened the liver and spleen were found to be mottled by yellowish specks, obviously abscesses. There was no evidence of metastases in the abdomen or in the lungs.

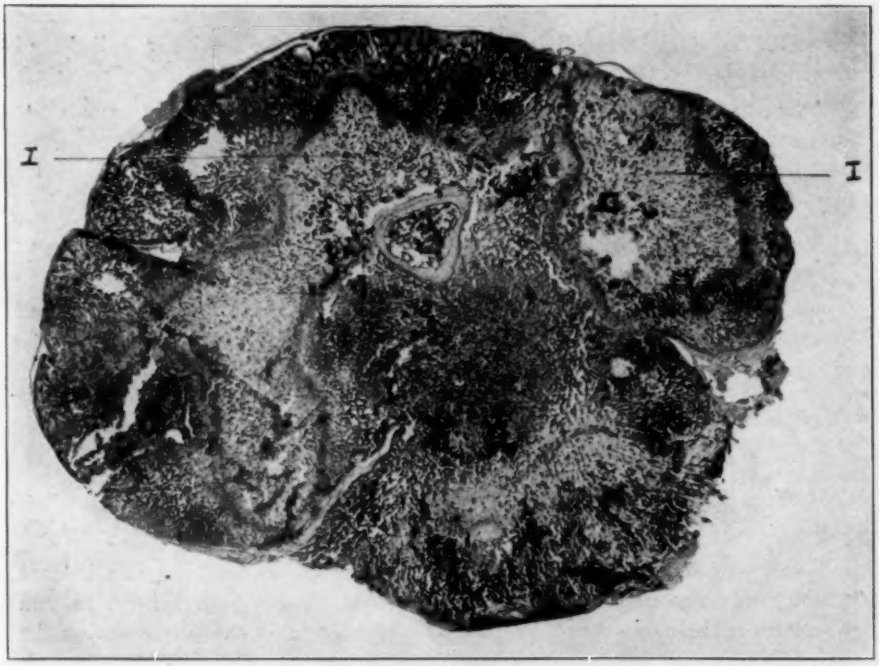

Fig. 2.—Photomicrograph of a horizontal section through the osteosarcoma; × 11. Near the center is seen a cross-section of the tibial shaft, the marrow cavity containing tumor bone. *I* indicates irregular areas of infarction in the extracortical portion of the tumor.

The skin over the left tibia had been pulled downward from above so that portions of the tumor could be bitten off with scissors for transplantation under aseptic conditions.

In the center of horizontal microscopic sections through the tumor the cross-section of the tibial shaft could be seen. The normal bone was living. A rather dense network of fine anastomosing trabeculae of tumor bone filled the marrow cavity. The spaces between these trabeculae contained fine branching spindle cells separated by wide intercellular spaces. The tumor mass about the tibia presented a similar histologic appearance, but within it were irregular confluent areas of infarction in which the bony trabeculae were in various stages of necrosis and

surrounded by necrotic spindle cells. These areas also presented varying degrees of polymorphonuclear infiltration. The peripheral margin of the tumor mass was smooth and circumscribed. The overlying muscles had been pushed outward and were only slightly infiltrated by tumor. The density of the new tumor bone varied from one portion of the section to the other. The fibula had been pushed outward for some distance from the tibia but was also included in the mass.

Examination of the liver showed diffuse acute pericholangitis and curious scattered areas of coagulation necrosis of the liver cells.

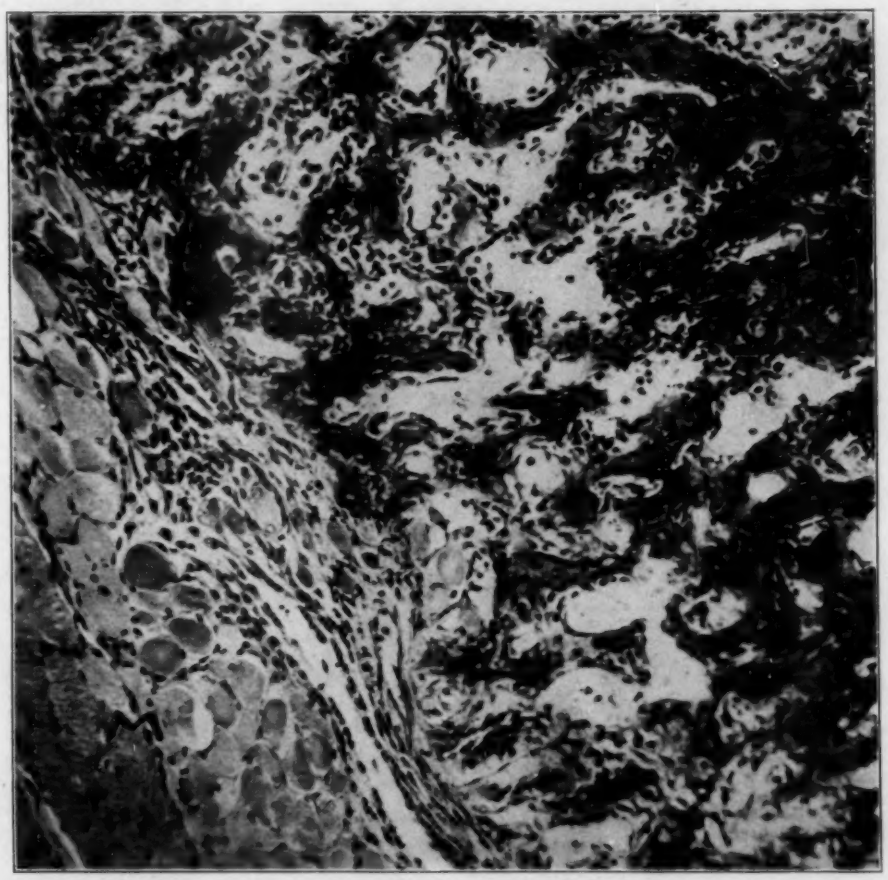

Fig. 3.—Photomicrograph of the peripheral portion of the osteosarcoma, showing beginning infiltration of the overlying muscles at *M*; × 250.

Attempted Transplantation.—As stated previously, the tumor-bearing animal suddenly became ill about forty-eight hours prior to being killed. Twelve white mice in apparent good health were inoculated with fragments of the tumor by means of a trocar inserted into the subcutaneous tissues of the back and intramuscularly in the thighs. During the following ten days nine of the animals sickened rapidly and died. The livers exhibited the same gross and microscopic appearance as the liver of the tumor-bearing animal. In the surviving three mice

the grafts also did not take, and the animals were quite ill for several days, dying two to three weeks later. In two of them a large cutaneous ulceration developed over the graft in the back. It is concluded that a highly infectious and lethal disease (with septicemia) developed in the tumor-bearing mouse a short time before it was killed and that this was transferred to the inoculated mice.

COMMENT

The histologic structure, the roentgenographic appearance and the rapidity of growth of the tumor described justify the diagnosis of osteosarcoma. That metastases were not present does not alter this view, because experience with the sarcomas produced by the carcinogenic hydrocarbons has shown that metastases do not develop before death in most cases and that when they do it is usually after the primary

Fig. 4.—Roentgenogram of a fibrosarcoma of the lower end of the femur of a rat; the growth developed twelve months after intramedullary implantation of a pellet of methylcholanthrene and cholesterol. Note the degree of osteolysis. The appearance is similar to that produced by such a tumor in man.

growth has become quite large—considerably larger in our experience than the osteosarcoma described here.

The fact that in this mouse the osteosarcoma arose from the bone into which the carcinogenic material had been implanted and after a prolonged latent period (which is to be expected from the observation on irradiation bone sarcomas) favors the assumption that the growth was due to the carcinogenic substance. In over two hundred mice from the same stock in this laboratory, which were observed for several months, spontaneous osteosarcomas were not encountered, although spontaneous mammary tumors developed in approximately from 10 to 15 per cent.

Because epidermoid carcinomas are produced when these compounds are applied to the skin and sarcomas develop after subcutaneous injections, it has been inferred that these hydrocarbons can produce any type of malignant tumor, depending on the tissues adequately exposed. However, final confirmation of this view must await further experimentation.

SUMMARY

An osteosarcoma (bone-forming sarcoma) developed in the tibia of a mouse which had received an intramedullary implantation of a mixture of 1,2-benzpyrene and cholesterol eight and one-half months previously. It would appear that this is the first instance recorded of the experimental production of an osteosarcoma by a chemical agent. Previously osteosarcoma and fibrosarcoma of bone have been produced experimentally only by irradiation.

Fig. 5.—Low power photomicrograph of the lesion shown in figure 4. The tumor is composed of small spindle cells, and there is no ossification of the mass. Practically all of the lower epiphysis of the femur and some of the metaphysis have been destroyed by the tumor. *C* indicates the cortex of the lower metaphysis; *PB*, new periosteal bone—"periosteal lipping"; *T*, fibrosarcoma, and *B*, small fragments of undestroyed bone and articular cartilage pushed out of place by expansile growth of the tumor.

Thus osseous tissue may be added to the list of tissues in which malignant degeneration has been produced by means of 1,2,5,6-dibenzanthracene, 1,2-benzpyrene and methylcholanthrene.

ADDENDUM

In one of another series of rats in which pellets of methylcholanthrene and cholesterol had been injected into the lower end of the left femur, a fibrosarcoma of bone developed after twelve months (figs. 4 and 5).

THE NICOLA OPERATION FOR RECURRENT DISLOCATION OF THE SHOULDER

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Because the older operations of capsulorrhaphy and Clairmont's muscle sling procedure for recurrent dislocation of the shoulder have not proved satisfactory, tenosuspensions have become a welcome substitute. Of these, the Nicola [1] procedure is likely to prove the best, because the operation, which consists of a suspension of the head of the humerus by passing the tendon of the long head of the biceps muscle through it, is sound anatomically and simple to perform. The modification herein suggested is designed to facilitate conducting the tendon through a newly formed channel in the head of the humerus and also to insure a snug relationship between the two, which is one of the most important details in preventing recurrence of the dislocation.

To insure uniformly good results from this operation, certain technical details must be rigidly adhered to. These are as follows:

1. The channel through the head of the humerus must begin in the bicipital groove about 1 inch (2.5 cm.) below the lesser tuberosity. It must run a course so that its other end will appear on the articular head of the humerus (in the line of direction of the long tendon) about ½ to ¾ inch (1.3 to 1.9 cm.) from the edge of the articular cartilage. This provides a maximum check to recurrent dislocation.

2. The tendon must become fixed in the tunnel in the head of the humerus after it is transplanted. To assure such fixation it is necessary that the tendon fit the channel snugly and that it be divested of synovial membrane; otherwise the tendon will slide in the channel and fray or wear until it breaks.

The incision is made from the clavicle just above the coracoid process downward in the line of the fibers of the deltoid muscle along its anterior margin for about 4 inches (10 cm.). The fibers are divided by blunt dissection down to the joint. The tendon of the long head of the biceps muscle is located and exposed by cutting the transverse ligament of the humerus which holds it in the groove. It is exposed completely up into the shoulder joint and downward to the upper edge of the tendon of the pectoralis major muscle as it is inserted on the external bicipital ridge, and the synovial membrane covering it is removed.

The elbow is flexed to an angle of 45 degrees and the long head of the biceps muscle is cut in a Z fashion ½ inch (1.3 cm.) above the point where it disappears

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From the Surgical Service of the Crown Heights Hospital.

1. Nicola, T.: Recurrent Dislocation of the Shoulder, Surg., Gynec. & Obst. **60**:545-546 (Feb.) 1935.

behind the tendon of the pectoralis major muscle. The distal end is prevented from disappearing behind this tendon by a stay suture passed through it or by grasping it with an Allis forceps.

A hole is drilled through the head of the humerus with a 4 mm. drill. This begins in the bicipital groove 1 inch (2.5 cm.) below the lesser tuberosity and is directed so that it comes out on the articular head in the line of the tendon, about ½ inch (1.3 cm.) from the edge of the articular cartilage. The ordinary tonsil snare, which has a shank 4.3 mm. in diameter, is easily forced through the channel by a rotary motion, and the wire loop is drawn down snugly on the end of the proximal portion of the tendon. The snare is then withdrawn, carrying the tendon through the channel with it. The snare is released, and the two ends of the tendon are united by chromic catgut in the ordinary manner used in tendon suture.

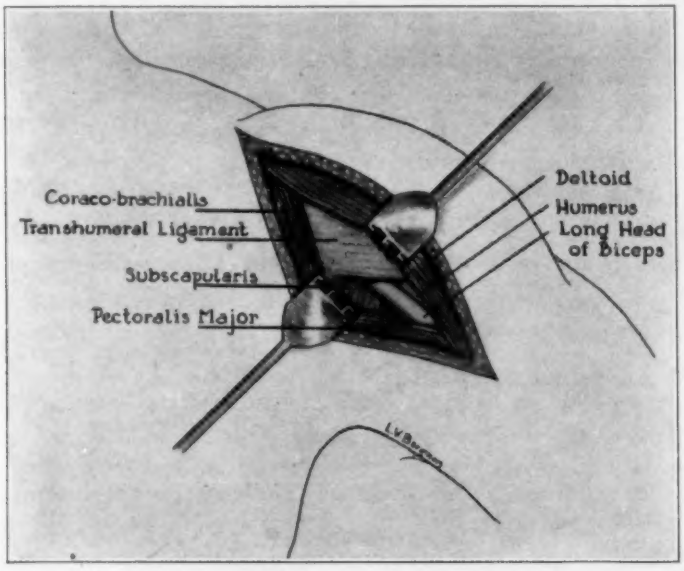

Fig. 1.—Position of the incision and approach to the tendon.

The arm is abducted to a right angle, and the transverse ligament is sutured to that part of the tendon which lies in the bicipital groove. The capsule, the split fibers of the deltoid muscle and the skin are united, and the shoulder is fixed by a Velpeau bandage with the elbow flexed at an angle of 45 degrees. It is kept in this position for two weeks, and then mobilization is begun.

The value of forcing the shank of the snare through the 4 mm. hole lies in the fact that the resultant channel will furnish a much more snugly fitting housing for the transpanted tendon, without undue cramping. The use of the wire obviates the necessity for the placement of a stay suture in the transplanted tendon, which has to be threaded on a probe so as to be guided through the tunnel.

Among other slight changes Willard [2] suggested that the distal end of the proximal portion of the tendon be anchored to the periostium

2. Willard, DeForest Porter: The Nicola Operation for Recurrent Dislocation of the Shoulder, Ann. Surg. **103**:438-443 (March) 1936.

at the point of its emergence from the drill hole. He also suggested the Z-shaped section of the tendon instead of the original transverse cut. Both of these additional precautions seem worth while.

To date the literature contains reference to thirty-seven operations by Nicola with only one recurrence and ten operations by Willard [2] with one recurrence. Hobart [3] published reports of two cases in which a combination of the Nicola and Clairmont operations was used. Without any evidence he stated that the Nicola procedure has not proved to be sufficient in all cases of severe strain.

D'Harcourt and Cuadrado [4] presented an extensive review of the whole subject of habitual dislocation of the shoulder and described in detail the various types of operative technic for its cure. Among them

Fig. 2.—Exposure of the tendon after division of the transverse ligament. The tendon was divided ½ inch (1.3 cm.) above where it disappears behind the tendon of the pectoralis major muscle.

they mentioned the Nicola operation but did not report any cases of their own. Norman [5] described the Nicola operation and mentioned that he used it in one case, but sufficient time has not elapsed for a conclusion to be drawn.

The operation as described here has been employed in three cases. While the operations were performed so recently that the end-results

3. Hobart, M. H.: Recurrent Dislocation of the Shoulder: Nicola Operation, with Report of Cases, J. Bone & Joint Surg. **15**:733-736 (July) 1933; The Hobart Operation: A New Combination Operation for Recurrent Dislocation of the Shoulder, ibid. **17**:1001-1004 (Oct.) 1935.

4. d'Harcourt, J., and Pérez Cuadrado, F.: Contribución al estudio de la luxación habitual de hombro, Rev. españ. de cir. **16**:173-201 (May-June) 1934.

5. Norman, J. S.: Recurrent Dislocation of the Shoulder, Colorado Med. **31**:85-86 (March) 1934.

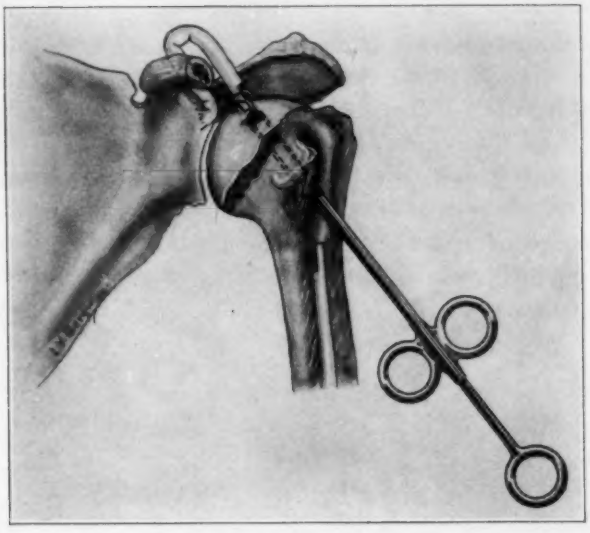

Fig. 3.—Tonsil snare introduced through the previously drilled channel in the head of the humerus ready to conduct the proximal portion of the tendon through.

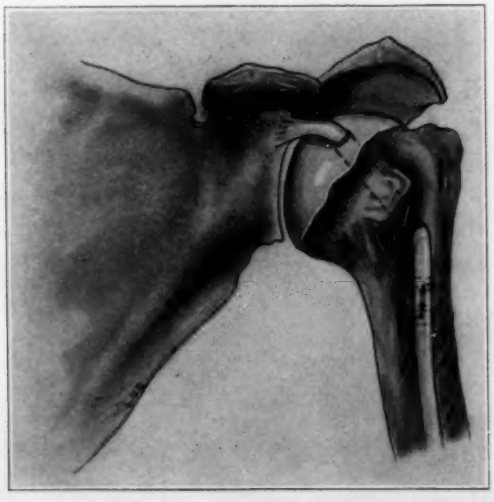

Fig. 4.—Ends of the tendon spliced after passage of the proximal portion through the head of the humerus.

cannot as yet be estimated, it seems significant that in case 1 there has been no recurrence, despite the many epileptic attacks the patient has had since operation.

REPORTS OF CASES

CASE 1.—M. P., a man aged 24, was admitted to the hospital on May 4, 1936, complaining of recurrent dislocations of the left shoulder. For the past four years he had been subject to epileptic attacks with unconsciousness. The attacks usually came on in the morning when he was asleep, but occasionally they occurred during the day, at which time there was no aura. The attacks lasted a few minutes. In the two years prior to admission the left shoulder had been dislocated eight times during the attacks. Operation was performed on May 5 according to the method described. At the time this report was written there had been no recurrence, despite the continuance of the frequent attacks of epilepsy, and the patient had full range of motion.

CASE 2.—P. R., a man aged 23, was admitted to the hospital on July 21, 1936, complaining of recurrent dislocations of the left shoulder. The first dislocation occurred seven years previously. Since then, there had been six dislocations. The last one occurred the day before admission and was reduced at the St. Vincent's Hospital. Operation was performed on July 22 at the Crown Heights Hospital according to the method described. At the time this report was written there had been no recurrence, and the patient had full range of motion.

CASE 3.—J. B., a man aged 20, was admitted to the hospital on Oct. 25, 1936, complaining of recurrent dislocation of the right shoulder. The first dislocation occurred about two months previously. Subsequently two more dislocations occurred, the last one taking place two days before admission. Operation was performed on October 26 according to the method described. The patient obtained full range of motion.

INGESTED FOREIGN BODY IN THE GASTRO-INTESTINAL TRACT

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AND
EUGENE A. GASTON, M.D.
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Our interest in the problem of the ingested foreign body which presents itself below the esophagus has been stimulated by 2 cases seen within recent months at the Boston City Hospital. In 1 of these the anterior wall of the stomach near the pylorus had been perforated by a chicken bone, giving rise to a clinical picture which was confused with that of acute cholecystitis. In the second case the clinical picture was confused with that of acute fulminating appendicitis with perforation and local peritonitis. At operation the terminal portion of the ileum was found to have been perforated by a bit of squash rind. These cases are reported in detail later.

In making this study we have limited our attention to those cases in which the foreign body, or the complications arising from it, have been located below the esophagus and above the rectum, since a foreign body in these extremities of the gastro-intestinal canal presents a specialized problem in instrumentation and treatment and is not ordinarily managed by the general surgeon. In addition, the vestigial structures of the gastro-intestinal tract have been excluded from more than passing consideration; the appendix, because foreign bodies in this vestige have been adequately dealt with in the older literature,[1] and Meckel's diverticulum, because of the relative rarity with which it has been involved.

From June 1, 1915, to Oct. 1, 1936, approximately 800 patients with a foreign body in the gastro-intestinal tract have been seen at the Boston City Hospital. The vast majority of these have been seen on the floor for accident cases, where they have been reassured and advised to return should symptoms arise. The records made on this floor are not suitable for the present study. Only 17 of the patients have been seen in the outpatient department, where records are kept which are suitable for study.

From the Fourth Surgical (Boston University Teaching) Service, Boston City Hospital.

1. Fowler, Royale Hamilton: Foreign Body Appendicitis, with Especial Reference to the Domestic Pin: An Analysis of Sixty-Three Cases, Ann. Surg. **56**:427-436, 1912.

Of the total patients seen, 88 appeared to the admitting physician to be in a sufficiently severe condition to warrant their admission to the hospital. The 88 hospitalized patients, together with the 17 seen in the outpatient department, make a total of 105 patients whose individual records were subjected to critical analysis.

HISTORICAL REVIEW

Ingested foreign bodies have played strange roles in the history of individuals and in the history of medicine. A shoe buckle came close to changing the history of the world. It was swallowed by Frederick Wilhelm I, in his fifth year on Dec. 31, 1692, and after an uneventful passage through his gastro-intestinal canal, it still lies in the Hohenzollern Museum at the Chateau of Monbijon. It was "a small silver buckle, one inch long, with the prong well protected by lying against the loop and at the other end a round knob wherewith to fix it to the strap—a very ordinary buckle, but had it not passed the larynx no Frederick the Great might have been begotten and the history of Europe would have been changed." [2]

The first appendectomy performed on a human subject was reported by Claudius Amyand in 1735. The patient, a boy of 11, had a discharging sinus of the right thigh which evidently communicated with an irreducible scrotal hernia. "On the interior of the hernia lay the appendix caeci which had been perforated by the point of a pin. The head, covered with much encrusted stone, remained within the appendix, acting as a ball-valve and allowing, at the most unexpected and inopportune moments, a copious discharge of fecal matter over the field of operation." [1] Mestivier [3] in 1759 is reported to have drained an abscess produced by a pin which had perforated the tip of the appendix.

The first gastrotomy for an ingested foreign body was reported by Mathis in 1602. A professional juggler, a man aged 36, had swallowed a knife, which remained in the stomach fifty-one days, causing "no great inconvenience." Adhesions between the stomach and the anterior abdominal wall were produced by "irritant plasters," and the knife was extracted through an incision made in this area.[4] Since then numerous reports have appeared in the literature describing remarkable

2. Layton, T. B.: Historic Foreign Body, Brit. M. J. **1**:24 (Jan. 4) 1930.

3. Mestivier, cited by Eitel, G. D.: Ingested Foreign Bodies in the Gastro-Intestinal Tract Requiring Surgical Removal, Minnesota Med. **18**:52-59 (Jan.) 1935.

4. Friedenwald, Julius, and Rosenthal, L. J.: A Statistical Report of Gastrotomies for Removal of Foreign Bodies from the Stomach, New York M. J. **78**:110-122, 1903.

foreign bodies that have been removed from the various segments of the gastro-intestinal tract. Swain [5] in 1895 reported the case of a young woman of 20 who for five years had suffered from daily bouts of vomiting. Examination revealed a mass which extended obliquely across the abdomen from the left costal margin down to the pelvis. At laparotomy the stomach was opened, and a hair ball weighing 5 pounds and 3 ounces (2,353 Gm.) was removed. "The stench evolved during the process of extraction was sickening." The mucous membrane at the pyloric end of the stomach was studded with circular raised patches of granulations, each about the size of a shilling. Recovery was uneventful except for a temporary gastric fistula, which closed after a Lembert suture was expelled from the wound. This is the third case on record in which a hair ball was removed by gastrotomy, and the hair ball represents the largest quantity of foreign material ever removed from the stomach at operation.

CLASSIFICATION OF FOREIGN BODIES

Since objects usually swallowed consist in the main of the trivialities common to every household, the physician is at once aware of the physical properties of the ingested foreign body and there is little need for an accurate classification. Briefly, it should be noted whether or not the swallowed object is long or short and, if long, whether one or both ends are pointed. Objects pointed at only one end are considerably less likely to cause complications during their passage through the gastro-intestinal canal which will necessitate surgical intervention than are objects pointed at both ends. It should also be noted whether the foreign body is single or multiple and in either event whether it is possible for the mass to pass the pylorus and navigate the curves of the duodenum. It has been stated that an object 5 cm. long is the largest that can be passed by a child of 2.[6]

The open safety pin presents a special problem and is subsequently dealt with at some length. If, as frequently happens, the open end presents at the pylorus with the point embedded in the wall of the stomach, there is little likelihood that it will pass, and at the same time there is a definite danger of perforation. With the spring end presenting into the pylorus, there is reason to hope that it will uneventfully traverse the length of the gastro-intestinal canal.

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5. Swain, Paul: Case of Gastrostomy: Removal of a Mass of Hair Weighing Five Pounds, Three Ounces from Stomach; Recovery, Lancet **1**:1581-1582, 1895.

6. Phelps, Kenneth, in discussion on Eitel,[15] p. 58.

ETIOLOGY OF SWALLOWED FOREIGN BODIES

Carelessness, as pointed out by Chevalier Jackson,[7] is the most frequent etiologic agent in the swallowing or aspiration of a foreign body. Carelessness in allowing ingestable foreign bodies to lie within reach of children, together with the bad example set by mothers and nurses of putting safety pins in the mouth during the dressing hour, are responsible for the majority of ingested foreign bodies in infants and young children. Dentures which cover much of the sensitive area of the mouth and allow a foreign body to be swallowed unwittingly with the food are responsible for many of the cases seen among adults. Multiple foreign bodies in the gastro-intestinal tract are usually seen in insane persons or have been swallowed with suicidal intent.

Achlorhydria is an important etiologic agent in the production of pathologic changes due to a swallowed bone. Knud Faber [8] found bones in the stool of 12 patients with achlorhydria after they had eaten fish. No bones were found in the stool of persons with normal gastric acidity after a similar meal, and he therefore concluded that small bones swallowed with the food are normally digested before damage can be done to the gastro-intestinal tract. Warbasse's case [9] lends support to this observation. The pearl and bone handles of 7 pocket knives removed from the stomach of a professional "human ostrich" were found to have been digested. Of the cases seen at the Boston City Hospital, asymptomatic achlorhydria was found in 1—case 1, in which the stomach had been perforated by a chicken bone.

FOREIGN BODIES PASSED PER VIAS NATURALES

The vast majority of foreign bodies ingested pass through the gastro-intestinal canal without producing symptoms or demonstrable pathologic change. Of the 800 cases seen at the Boston City Hospital, perforation occurred in only 9—an incidence of about 1 per cent. That the incidence of perforation is much less than is represented by this figure is evident when one realizes that a great many persons who have ingested a foreign body never come under the observation of the physician, either because the fact that the foreign body has been swallowed is not appreciated by the patient or because the lack of symptoms makes the consultation with a physician seem unnecessary.

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7. Jackson, Chevalier, and Jackson, Chevalier L.: Diseases of the Air and Food Passages of Foreign Body Origin, Philadelphia, W. B. Saunders Company, 1936, pp. 272-282.

8. Faber, Knud, cited by Norinder, E.: Zur Kenntnis der Komplikationen bei Fremdkörpern im Magen (Ein Fall von perforierender Fischgräte), Acta chir. Scandinav. **76**:136-146, 1935.

9. Warbasse, James P.: Tetany, and Foreign Bodies in the Stomach, Ann. Surg. **40**:909-915, 1904.

In a collected series of 1,184 cases of ingested foreign body, Wölfler and Lieblein [10] found that the object had passed naturally in 427 and that in an additional 44 it was no more than an incidental finding at autopsy. They also stressed the point that these figures do not represent a true picture of the percentage of ingested foreign bodies which pass without causing symptoms.

The medical literature is replete with remarkable examples of the types and numbers of foreign bodies passed per vias naturales. Vinson and Deissler [11] recorded the case of a professional tack swallower who had been plying his trade for seventeen years without suffering untoward symptoms. Roentgen examination showed the stomach and intestine to be literally filled with tacks. Habbe [12] reported a case in which he watched, by means of serial roentgenograms, the passage of a double-edged safety razor blade through the gastro-intestinal canal. The patient remained free from symptoms, and the blade was eventually removed from the rectum through a proctoscope. Johnstone [13] recorded the case of a man who had 13 operations for the removal of foreign bodies from various portions of the gastro-intestinal tract. The foreign bodies were swallowed during a prolonged period as a stage performer and included such objects as nails, screws, fountain pen, spoon handles, etc.

In an effort to determine when one may expect the passage of a foreign body by the natural route, the 69 cases at the Boston City Hospital were subjected to critical analysis. From table 1 it will be seen that the average time required for the passage of all types of foreign bodies seen was five and one-tenth days, with extremes of one day in a 10 month old infant who had swallowed a common pin to thirty-seven days in a 2½ year old child who had swallowed a nail. It will further be seen that in general there is no correlation between the age of the patient and the time required for a foreign body to traverse the gastro-intestinal canal.

In table 2 the same cases are classified into groups according to the physical characteristics of the foreign bodies swallowed. These groups include foreign bodies which are pointed at one end only, foreign bodies which are pointed at both ends and nonsharp foreign bodies. Because

10. Wölfler, A., and Lieblein, V.: Die Fremdkörper des Magendarmkanals des Menschen, in von Billroth, T., and Luecke, G. A.: Deutsche Chirurgie, Stuttgart, Ferdinand Enke, 1909, no. 46B.

11. Vinson, P. P., and Deissler, Karl: (*a*) Management of Patients with Foreign Bodies in Stomach, Proc. Staff Meet., Mayo Clin. **9**:289-290 (May 16) 1934; (*b*) Treatment of Patients with Foreign Bodies in Esophagus or Stomach, Am. J. Digest. Dis. & Nutrition **1**:357-359 (Aug.) 1934.

12. Habbe, cited by Eitel.[15]

13. Johnstone, I. Lloyd: Swallowing Foreign Bodies for a Livelihood, Brit. M. J. **2**:546 (Sept. 21) 1935.

of the frequency with which it is seen and its peculiar physical properties, the open safety pin is considered as a separate group. As will be seen, the nonsharp foreign bodies required an average of four and eight-tenths days to traverse the gastro-intestinal tract; those pointed at one end only required an average of five and eight-tenths days, while those

TABLE 1.—*Time Required for Passage of Foreign Bodies per Via Naturales*

Type of Foreign Body	No. of Cases	Average Age	Extremes of Age		Time Required to Pass		
			Youngest	Eldest	Average	Shortest (Age)	Longest (Age)
Straight pin	15	14.1 yr.	10.0 mo.	28 yr.	3.5 days	1 day (10 mo.)	7 days (1.8 mo.)
Open safety pin	11	4.4 yr.	9.0 mo.	12 yr.	4.6 days	1.5 days (10 mo.)	7 days (18 and 5 yr.) (2 cases)
Coin (1, 5 and 25 cent)	11	5.4 yr.	2.0 yr.	9 yr.	4.0 days	3 days (6 yr.)	5 days (5 yr.)
Nail	7	5.9 yr.	1.5 yr.	10 yr.	12.0 days	3 days (10 yr.)	37 days (2.5 yr.)
Tack	7	6.8 yr.	4.0 mo.	35 yr.	5.3 days	5 days (4 cases)	6 days (2 cases)
Closed safety pin	6	3.8 yr.	2.0 mo.	8 yr.	5.3 days	3 days (2 mo.)	7 days (2 yr.)
Screw	3	4.0 yr.	2.0 yr.	6 yr.	2.5 days	1 day (2 yr.)	4 days (4 yr.)
Marble	3	6.0 yr.	4.0 yr.	7 yr.	6.5 days	6 days (7 days)	7 days (4 yr.)
Sharp glass (fragments)	3	15.8 yr.	1.5 yr.	39 yr.	2.0 days	2 days (7 yr.)	2 days (39 yr.)
Needle	3	21.0 yr.	4.0 yr.	38 yr.	7.0 days	4 days (4 yr.)	10 days (21 yr.)
Pen point	2	4.8 yr.	0.5 yr.	9 yr.	5.0 days	5 days (9 yr.)	5 days (0.5 yr.)
Staple	2	4.0 yr.	2.0 yr.	6 yr.	6.0 days	4 days (6 yr.)	8 days (2 yr.)
Shoe buckle	2	6.0 yr.	4.0 yr.	8 yr.			
False teeth	2	46.5 yr.	30.0 yr.	63 yr.			
Toy whistle	2	4.8 yr.	2.5 yr.	7 yr.	7.0 days	6 days (2.5 yr.)	8 days (7 yr.)
Campaign button	2	5.0 yr.	4.0 yr.	6 yr.	5.5 days	4 days (6 yr.)	7 days (4 yr.)
Phonograph needle	2	5.0 yr.	5.0 yr.	5 yr.			
Key	1	18.0 yr.	.....	.....	3.0 days		
Wood splinter (tooth pick)	1	3.0 yr.					
Picture hanger	1	6.5 yr.	.....	.....	4.0 days		
Cup hook	1	2.0 yr.	.....	.....	5.0 days		
Jack stone	1	4.0 yr.	.....	.....	4.0 days		
Nonsharp steel	1	3.0 yr.					
Total	89	.....	.....	.....	5.1 days		

pointed at both ends required an average of seven days. Strangely enough, the open safety pins required an average of but four and six-tenths days for passage through the gastro-intestinal tract, a fact which is probably accounted for in that those pins which pass have the spring end foremost, while the two after-coming tips spread out in wedge fashion and may become entagled in the intestinal content and be carried along with it. While the various groups are not large enough from which to draw definite comparisons, it seems evident in evaluating the

individual case that if the foreign body has not passed out of the gastro-intestinal tract by the end of seven days, it is in all likelihood impacted somewhere along the route, and complications are likely to develop.

Serial roentgenograms should be made in every case of ingested foreign body. If by this means it is evident that the foreign body is making uninterrupted progress along the gastro-intestinal tract, one is relatively safe in delaying surgical intervention. However, as Jackson [7] has pointed out, if the foreign body remains in the same location in

TABLE 2.—*Time Required for Passage of Foreign Bodies Per Vias Naturales According to Groups*

Class of Foreign Body	No. of Cases	Average Age, Yr.	Average Time Required to Pass, Days	Average Time Required to Pass for Each Group, Days
I Pointed at one end				
Straight pin	15	14.1	3.5	
Nail	7	5.9	12.0	
Tack	7	6.8	5.3	
Screw	3	4.0	2.5	
Fragments of glass	3	15.8	2.0	
Pen point	2	4.8	5.0	
Staple	2	4.0	6.0	
Campaign button	2	5.0	5.5	
Phonograph needle	2	5.0		
Cup hook	1	2.0	5.0	
Average	44	9.0	5.8	5.8
II Pointed at both ends				
Needle	3	21.0	7.0	
Wood splinter	1	3.0		
Average	4	14.0	7.0	7.0
III Open safety pin (pointed wedge)	11	4.4	4.6	4.6
IV Nonsharp foreign bodies				
Coin	11	5.4	4.0	
Closed safety pin	6	3.8	5.3	
Marble	3	6.0	6.5	
Shoe buckle	2	6.0		
False teeth	2	46.5		
Toy whistle	2	4.8	7.0	
Key	1	18.0	3.0	
Picture hanger	1	6.5	4.0	
Jack stone	1	4.0	4.0	
Nonsharp steel	1	3.0		
Average	30	8.2	4.8	4.8

relation to the viscerae (not necessarily in relation to the bony landmarks) for five days or longer, operation should be considered. If abdominal tenderness develops while the patient is under observation after having swallowed a foreign body, operation should be resorted to immediately.

TYPES OF INGESTED FOREIGN BODIES REQUIRING SURGICAL INTERVENTION

Foreign Bodies Causing Perforation of the Gastro-Intestinal Tract.—In reviewing the literature concerning perforation of the gastro-intestinal tract by an ingested foreign body, one frequently comes across

the statement that the stomach and the duodenum are but rarely perforated, while the colon, particularly at the flexures, is the most frequent site of perforation.[14] In an effort to determine the accuracy of this statement, an extensive review of the reported cases was made. For reasons previously stated, cases of perforation of the esophagus, Meckel's diverticulum, appendix and rectum were excluded. With these exceptions, a total of 71 cases, including 9 seen at the Boston City Hospital and not previously reported, were collected and analyzed (table 3). Of the 71 cases, the stomach was found to have been perforated in 26, or 36.6 per cent; the duodenum in 10, or 13.9 per cent; the small intestine in 12, or 16.6 per cent; the cecum in 11, or 15.3 per cent, and the colon in 12, or 16.6 per cent. The perforation of the large intestine occurred in the sigmoid flexure in 6 cases.

In evaluating these figures it is necessary to stress again the point that it is impossible to arrive at accurate conclusions regarding the frequency with which various portions of the gastro-intestinal tract are perforated by an ingested foreign body. This is due to the inaccessibility of many of the reported cases and to the fact that a great many cases are not reported. However, from the foregoing figures it is fair to state that the stomach is probably perforated as frequently as is any portion of the gastro-intestinal tract. Perforation of the stomach by a foreign body carries with it the same implications as does perforation of a peptic ulcer, and surgical intervention should be no less prompt.

Foreign bodies perforate the gastro-intestinal tract by several methods: A pointed foreign body may be pushed through the stomach or intestinal wall by peristaltic activity. Such a perforation gives rise to symptoms of spreading peritonitis of acute onset. At operation no adhesions are found walling off the inflammatory process. In table 3 this has been designated as "acute perforation." In the series of 71 collected cases, 19 (26.4 per cent) were of this variety. A nonsharp as well as a sharp foreign body may penetrate the gastro-intestinal wall by means of ulceration due to pressure necrosis. Such a perforation becomes walled off with adhesions which limit the extent of the inflammatory reaction and give rise to symptoms of a subacute or a chronic nature. At times there is such an over-production of granulation tissue that large tumors are found which may readily be mistaken for neoplastic disease and in extreme cases may cause intestinal obstruction.

14. (*a*) Bearse, Carl: Fishbones as a Cause of Intestinal Perforation, New England J. Med. **201**:885-886 (Oct. 31) 1929. (*b*) Ginzburg, Leon, and Beller, A. J.: The Clinical Manifestations of Non-Metallic Perforating Foreign Bodies, Ann. Surg. **86**:928-939 (Dec.) 1927. (*c*) Stone, Harvey B., and Owings, James C.: Perforation of the Stomach by a Fish Bone, Am. J. Surg. **25**:180-182 (July) 1934.

This type of perforation has been labeled herein "chronic perforation" and was found in 16 cases (22.5 per cent). Finally, chronic perforation may go on to abscess formation, as occurred in 25 (34.7 per cent) of the cases. In 11 (15.3 per cent) cases the type of perforation was not evident.

From table 3 it will be seen that acute perforation of the gastro-intestinal tract is most likely to occur in the small intestine, with the cecum the next most likely site. Chronic perforation and abscess formation are most likely to occur in the sigmoid colon, cecum and stomach.

The treatment of perforation of the gastro-intestinal tract by a foreign body is purely surgical. In the case of an acute perforation the foreign body should be removed. The site of perforation should

TABLE 3.—*Site of Perforation of the Gastro-Intestinal Tract by Foreign Bodies*

Organ Perforated	Acute Perforation		Chronic Perforation		Abscess Formation		Not Stated		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Stomach	4	15.4	7	27.0	10	38.5	5	19.2	26	36.6
Duodenum	3	30.0	4	40.0	0	0.0	3	30.0	10	14.1
Jejunum	0	0.0	1	100.0	0	0.0	0	0.0	1	1.4
Ileum	3	42.9	1	14.3	2	28.5	1	14.3	7	9.8
Small intestine (portion not stated)	3	....	0	0.0	1	....	0	0.0	4	5.6
Total small intestine	6	50.0	2	16.6	3	25.0	1	8.3	12	16.9
Cecum	4	36.4	0	0.0	5	45.4	2	18.2	11	15.5
Ascending colon	0	0.0	1	100.0	0	0.0	0	0.0	1	1.4
Transverse colon	1	50.0	0	0.0	1	50.0	0	0.0	2	2.8
Hepatic flexure	0	0.0	0	0.0	1	100.0	0	0.0	1	1.4
Descending colon	0	0.0	1	100.0	0	0.0	0	0.0	1	1.4
Splenic flexure	0	0.0	0	0.0	1	100.0	0	0.0	1	1.4
Sigmoid flexure	1	16.6	1	16.6	4	66.6	0	0.0	6	8.4
Total large intestine (excluding cecum)	2	....	3	....	7	....	0	0.0	12	16.9
Total	19	26.4	16	22.5	25	34.7	11	15.3		

be closed by means of a purse-string or other suture, and drainage of the peritoneal cavity may or may not be instituted, according to the location of the perforation. If the perforation is in the stomach or the upper portion of the jejunum and the symptoms are of less than ten hours' duration, drainage is not indicated. If the perforation is in the ileum or colon, drainage should always be instituted.

Of the 9 cases of perforation by a foreign body seen at the Boston City Hospital, 6 were of the acute type.

CASE 1.—Mrs. J. M., a 54 year old housekeeper, was admitted to the surgical service on Nov. 12, 1936, complaining of abdominal pain of sixty hours' duration. On being questioned, she stated that three and a half years previously she noted the gradual onset of intolerance to certain foods, especially fatty and fried foods, together with gaseous eructations after meals. At the same time she noted the onset of occasional aching pain in the right side of the hypochondrium. All symptoms had increased during the past year.

Six days before admission, she noted the gradual onset of a mild shooting pain in the right side of the hypochondrium which radiated downward to the region of

the right lower quadrant and which was decidedly different from the discomfort which she had previously noted. The pain became gradually and progressively worse until sixty hours before admission, when she was awakened from a sound sleep by a severe exacerbation of the same type of pain. It was aggravated by physical exertion, particularly by walking, and was noted to be more severe when she lay on her left than when she lay on her right side. The pain continued unabated until the patient's admission to the hospital and was accompanied by the vomiting of bitter, bile-tinged, watery material. At no time did she note blood in the vomitus or bloody, tarry or clay-colored stools. There were no chills, fever or diarrhea and no history of jaundice.

Physical examination revealed a rather obese woman who appeared to be in great pain. The temperature was 98.6 F., the pulse rate 72 and the respiratory rate 20. The blood pressure was 120 systolic and 70 diastolic. Except for the abdomen, the results of the physical examination were essentially negative. There was a well healed lower midline scar from the previous uterine suspension. Tenderness and mild involuntary muscle spasm were noted over the entire right upper quadrant, with the point of maximum tenderness in the midclavicular line, 2 inches (5 cm.) below the costal margin. No masses or viscerae were felt, and the results of the pelvic and rectal examinations were within normal limits. The red blood cell count was 4,250,000. The hemoglobin content 90 per cent and the white blood cell count 9,000. The urine was normal. The Hinton test was negative. The stools were negative for occult blood and parasites. Analysis of the gastric contents revealed no free acid after the alcohol meal or after the injection of histamine. The total acid content after the injection of histamine was 2 units.

Roentgenograms of the region of the gallbladder after the oral administration of the dye showed no filling of the gallbladder. A small vertical shadow opposite the interspace between the first and the second lumbar vertebrae (fig. 1) was noted, but its significance was not realized until the pictures were reviewed after the operative findings were known.

After three days of preoperative preparation, during which time there was no abatement of symptoms, operation was performed through a right upper rectus incision. When the peritoneal cavity was opened, a diffuse injection was noted on the anterior surface of the stomach and the transverse colon, with a small amount of peritoneal fluid. Further exploration revealed a minute perforation of the wall of the stomach on the anterior surface just proximal to the pyloric ring and about 1 cm. below the lesser curvature. Through this perforation protruded a fragment of chicken bone, 3.6 cm. in length (fig. 2). This was removed, and the defect was closed with a purse-string suture of chromic catgut. Exploration of the gallbladder revealed it to be small, thickened and bound down by numerous fibrous adhesions. No stones were present. Because the patient's condition was excellent and because she had a definite history of disease of the gallbladder of long standing, the adhesions were freed, and the gallbladder was removed from above downward. A cigaret drain was placed to Morrison's pouch, and the wound was closed in layers around the drain.

Postoperatively, the patient had an entirely uneventful convalescence. She was discharged home on the sixteenth postoperative day. One month after discharge she was entirely free from symptoms, and a meal of barium sulfate revealed no demonstrable pathologic process in the stomach or duodenum.

CASE 2.—Mrs. G. P., a white housewife aged 52, was admitted to the surgical service on Nov. 29, 1936, complaining of abdominal pain of seven hours' duration.

The onset was rather sudden, and at first the pain was localized to the region of the umbilicus, but it spread steadily until it involved the entire abdomen. Two hours after the onset the patient vomited, after which the pain became more severe and seemed to be somewhat worse on the right side. Examination revealed the temperature to be 98.8 F., the pulse rate 90 and the respiratory rate 18. The results of the examination were essentially negative, except for the abdominal findings.

Fig. 1.—Roentgenogram of the region of the gallbladder showing, within the circle, the perforating foreign body.

Fig. 2.—Photograph of a chicken bone which perforated the stomach.

There was marked tenderness and muscle spasm throughout the right lower quadrant and in the region of the umbilicus, with the point of maximum tenderness just to the right of the umbilicus. Pelvic and rectal examinations gave negative results. A preoperative diagnosis of acute appendicitis was made, and the patient was operated on soon after admission.

At operation, performed through a right lower rectus incision, the appendix was found to be normal. About 4 feet (120 cm.) proximal to the ileocecal valve,

a piece of squash rind was found to have perforated the ileum. There was a surrounding localized peritonitis. The foreign body was removed, and the defect in the bowel was closed with a double tier of linen sutures. A drain was placed to the pouch of Douglas, and the wound was closed in layers.

The patient made an uneventful convalescence and was discharged home on the twenty-first postoperative day. When seen in the follow-up clinic one month later, she was entirely free from sypmptoms.

CASE 3.—R. C., a 7 month old boy, was admitted to the hospital on May 20, 1923. The mother stated that two days before admission the child had swallowed an open safety pin. He gagged a little at the time but had suffered no other symptoms. The results of the physical examination at the time of admission were negative. The abdomen was soft, symmetrical and tympanitic. There was no tenderness and no muscle spasm, and no masses were palpable. A roentgenogram of the abdomen showed an open safety pin, with the point directed downward, probably in the pyloric end of the stomach. The child was observed in the ward for eleven days, when a second roentgenogram showed no change in the position of the pin. Operation was performed the following day through a high midline incision. The open safety pin was located at the duodenojejunal flexure and was found to have perforated the wall of the bowel at this point. An incision was made in the intestinal wall, the pin was removed and the incision in the bowel was closed in the transverse diameter. The abdominal wall was closed in layers around a cigaret drain. Shortly after the operation, the patient began to fail. Despite vigorous supportive treatment, he died thirty-six hours postoperatively.

This case illustrates the necessity for the closest possible clinical and roentgen studies in cases of ingested foreign body. Undoubtedly the pin had perforated some time prior to operation, and had the operation been resorted to earlier the patient would no doubt have lived.

CASE 4.—J. H., an 8 year old school boy, was admitted to the hospital on April 30, 1923, complaining of pain in the right side of the abdomen of twenty-four hours' duration. The pain had been of rather sudden onset and was constant; it was worse in the right lower quadrant. The patient was given castor oil at the time of the onset and had had watery diarrhea since. There was no nausea or vomiting. Physical examination revealed a well developed and well nourished boy of 8 who appeared to be acutely ill. The temperature was 100 F., the pulse rate 100 and the white blood cell count 12,000. There was marked tenderness without muscle spasm in the right lower quadrant of the abdomen, and a tender mass was palpable just above Poupart's ligament on the right side. Soon after the patient's admission to the hospital the abdomen was explored through a right lower rectus incision. The appendix was normal and was removed in the usual fashion. Further exploration revealed a deeply injected piece of small bowel through which a wooden splinter had perforated. The surrounding intestine and mesentery were covered with fibrin, but there was no free pus. The foreign body was removed, and the opening in the bowel was closed with a purse-string suture. The abdominal wall was closed around a drain placed to the region of the perforation. The patient made an entirely uneventful convalescence and was discharged home on the fourteenth postoperative day.

CASE 5.—G. L. F., a 34 year old schoolteacher, was admitted to the hospital on Aug. 19, 1936, complainng of being weak, run down and overworked for the past

week. The morning of the day of entry, feeling depressed, he attempted to commit suicide by swallowing foreign bodies. Physical examination on admission gave negative results. A roentgenogram of the abdomen at this time revealed 11 pieces of bed spring scattered through the gastro-intestinal tract with five grouped at the cecum. At 5 p. m. on the day of admission the patient seemed to be in great pain. At 6 p. m. the pain had increased, and the abdomen showed definite signs of spreading peritonitis beginning in the right lower quadrant. At 7:30 p. m. operation was performed through a lower midline incision. A large amount of cloudy fluid was present in the peritoneal cavity. A piece of bed spring was found to have perforated the cecum. The site of perforation was enlarged, and six pieces of bed spring were removed. Four more pieces of bed spring were found in the sigmoid flexure and were removed through a small opening in the bowel. A lead pencil and 4 matches were also removed from the sigmoid flexure. The openings in the cecum and the sigmoid flexure were closed with purse-string sutures, and the abdomen was closed around a drain placed in the pelvis. One hour after operation the patient died, having failed to rally to vigorous supportive treatment.

CASE 6.—P. S., a 32 year old man, was admitted to the hospital on Oct. 8, 1918, complaining of abdominal pain of seven days' duration. The pain had been localized to the right lower quadrant and had been accompanied by cough, which had aggravated the pain. The pain was sharp and constant. There had been no vomiting or change in the bowel habits. Physical examination revealed a well developed and well nourished white man who appeared to be acutely ill. There was marked tenderness throughout the entire right side of the abdomen, with the point of maximum tenderness in the right lower quadrant. Muscle spasm was present over the right side. On the day of admission the patient was operated on through a right lower rectus incision. The appendix appeared to be normal but was removed in the usual manner. On further exploration the transverse colon was found to have been perforated by a sharp piece of bone or wood, 1½ inches (3.7 cm.) long, which was partially inside the lumen. The foreign body was removed, and the perforation was closed with a purse-string suture. The abdomen was closed around a drain placed to the site of perforation. The patient made an entirely uneventful convalescence and was discharged home on the thirteenth day postoperatively.

Two cases of chronic perforation of the gastro-intestinal tract have been seen at the Boston City Hospital.

CASE 7.—J. C., a 45 year old man, was admitted to the Boston City Hospital on Feb. 20, 1935, complaining of abdominal pain. He dated the onset of his present illness to twenty-four hours before admission. However, he stated that for four days, ending one month before admission, he had suffered from abdominal cramps and diarrhea. He attributed this to food, as other members of his family had suffered from the same symptoms at that time. At the end of this four day period he returned to work and felt well until five days before admission when he again began to suffer from abdominal cramps and diarrhea. At the end of four days his symptoms again disappeared without medical attention. Twenty-four hours before admission he felt so well that at noon he ate a hearty meal of spaghetti. At 6 p. m. on the same day he noted the rather sudden onset of severe epigastric pain, which was sharp and stabbing and nonradiating. By 2 a. m. the pain had become so severe that a physician gave him a hypodermic injection, with relief. By 8 a. m.

on the following day the pain had returned in all of its severity and continued to become progressively worse until the patient's admission to the hospital at noon.

Physical examination revealed a well developed and well nourished man who was in great pain. There was marked tenderness in the epigastrium with involuntary muscle spasm throughout the upper portion of the abdomen. The tenderness was somewhat more marked just to the right of the midline. Rectal examination gave negative results. The white cell count was 20,000 per cubic millimeter of blood. The urine was normal, and fluoroscopy of the abdomen showed no evidence of pneumoperitoneum.

Operation was performed through a right upper rectus incision soon after the patient's admission. There was a moderate amount of clear serous fluid in the peritoneal cavity. A piece of wood, 1½ inches long, was found near the stomach. The omentum was adherent to the anterior wall of the pylorus and, more particularly, to the first portion of the duodenum, and the point of perforation could not be found, undoubtedly being under the adherent omentum. A drain was placed to the region of the pylorus, and the wound was closed in layers around the drain.

The postoperative convalescence was complicated by paralytic ileus secondary to a subfascial abscess of the wound.

During his convalescence the patient identified the small sliver of wood as being a part of the seasoning used in the preparation of the spaghetti eaten six hours before the onset of his acute symptoms. In view of the completeness with which the perforation was walled off, it seems likely that penetration of the duodenum had been going on for some time, causing the recurrent bouts of indigestion, and that perforation finally occurred twenty-four hours before admission into a field which was already well walled off by omentum. The vegetable seasoning (dried thyme) was used frequently in the patient's food, and the bit causing the perforation may have been swallowed some time before.

The patient was seen twenty months after his discharge from the hospital, at which time he was enjoying excellent health. Appetite and digestion were normal, and he had gained 20 pounds (9.1 Kg.) since the operation. Serial roentgenograms of the gastro-intestinal tract showed no evidence of a pathologic process in the stomach or duodenum.

Cases 1 and 7 illustrate the complete healing of the stomach and duodenum, respectively, after perforation of their walls by foreign bodies. Roentgenograms of the gastro-intestinal tract in each case failed to demonstrate scarring or any other pathologic process.

CASE 8.—W. B., a 15 year old school boy, was admitted to the hospital on Jan. 24, complaining of pain in the left lower abdominal quadrant of one month's duration. One month before admission he had accidentally swallowed a common pin. Two days later he began to suffer with the pain, which persisted until the time of entry. Physical examination revealed a well developed and well nourished boy in no great distress. The temperature was 98.8 F. and the pulse rate 80. The abdomen was soft and symmetrical throughout. There was slight tenderness throughout the entire left side of the abdomen, which was not well localized. There was no muscle spasm, and no masses were felt.

Roentgen examination revealed a long pin in the descending colon, which could be seen piercing the wall of the bowel.

Twenty-four hours after admission the patient was operated on through a lower left rectus incision. The pin was found protruding through the wall of the descend-

ing colon, with the point foremost. An adjacent loop of ileum was adherent at the point of perforation and had also been pierced. The pin was removed, the wounds of the colon and ileum were closed with purse-string sutures and the abdominal wall was closed in layers around a drain.

Convalescence was entirely uneventful, and the patient was discharged home on the eleventh postoperative day.

Only 1 case of perforation with abscess formation has been seen at the Boston City Hospital.

CASE 9.—S. B., a 42 year old dressmaker, was admitted to the urologic service of the Boston City Hospital on Sept 30, 1931, complaining of pain of three weeks' duration in the right lower quadrant of the abdomen. The pain began in the right lower quadrant and later extended upward into the right flank. There had been no nausea, vomiting or diarrhea and no definite urinary symptoms.

Physical examination revealed an obese woman in no acute distress. There was tenderness throughout the right side of the abdomen and in the right flank. There was no muscle spasm. There was some tenderness in the right vault on vaginal examination. The temperature was 100 F., the pulse rate 110 and the respiratory rate 20. On microscopic examination the urine was found to be loaded with pus cells and to contain rare red blood cells.

A retrograde pyelogram showed stones in the pelvis of the right kidney, and these, together with the concomitant urinary infection, were thought to be responsible for the symptoms. During the next three days the temperature continued to rise, and a mass was finally felt in the right lower quadrant, approximately 3 inches (7.6 cm.) in diameter, which was tender and fixed. A preoperative diagnosis of appendical abscess was made, and operation was performed through a right lower rectus incision. After the peritoneal cavity had been well walled off, the abscess cavity was broken into, with the escape of foul-smelling pus. A common pin was found in the cavity. No effort was made to find the site of perforation; the abscess cavity was drained, and the abdominal wall was closed around the drain.

Convalescence was complicated by bronchopneumonia of the lower lobe of the right lung, from which the patient recovered after a long illness. The wound healed satisfactorily without the development of a fecal fistula.

It is worth noting that in none of the reported cases of perforation by a foreign body with abscess formation has the actual site of perforation been found and in none of the cases has a fecal fistula developed after drainage of the abscess.

In the 9 cases of perforation by a foreign body seen at the Boston City Hospital there were 2 deaths, a mortality of 22.2 per cent. These cases and those reported in the literature make up a series of 57 cases in which the end-results are known (table 4). As will be seen, the average mortality for the entire group was 14 per cent. The group of cases in which perforation of the stomach occurred carried the highest mortality (28 per cent), and in this group the cases in which there was abscess formation gave the highest percentage of mortality. The mortality for the cases in which perforation of the cecum occurred was 22.2 per cent; both deaths in this group were in cases in which acute

perforation occurred. The group in which perforation of the small bowel occurred commanded a mortality of 20 per cent, while, strangely enough, there were no deaths in 9 cases in which the large bowel (exclusive of the cecum) had been perforated.

Of the many thousands of cases of appendicitis seen at the Boston City Hospital, there is no record of a case in which the appendix had been perforated by a foreign body. This is rather remarkable in view of the not infrequent reports seen in the older surgical literature.[1] Only 7 cases of perforation of Meckel's diverticulum have been reported in the literature.[15] No such case has been seen at the Boston City Hospital.

TABLE 4.—*Result of Operation for Perforation in Cases in Which Result is Known*

Part of Gastro-Intestinal Tract	Acute Perforation, No. of Cases	Chronic Perforation, No. of Cases	Abscess Formation, No. of Cases	Not Stated, No. of Cases	Total Cases	Mortality for All Types of Perforation, %
Stomach	..	..	..	..	..	28.0
Recovery	3	8	7	..	18	
Death	1	3	3	..	7	
Duodenum	..	..	..	..	..	0.0
Recovery	2	2	..	..	4	
Death	0	0	..	..	0	
Small bowel	..	..	..	..	..	20.0
Recovery	5	2	1	..	8	
Death	1	0	1	..	2	
Cecum	..	..	..	..	..	22.2
Recovery	1	1	4	1	7	
Death	2	0	0	0	2	
Large bowel (exclusive of cecum)	..	..	..	..	..	0.0
Recovery	2	2	5	..	9	
Death	0	0	0	..	0	
Average mortality					57	14.0

Wölfler and Lieblein [10] found 35 cases in which foreign bodies had been involved in the contents of various types of hernia. There was abscess formation in 7 of these cases. Ginzburg and Beller [14b] have observed 2 such cases. Reports of this type of case are comparatively rare, and none have been seen at the Boston City Hospital.

It is interesting to speculate as to the possible relationship of a foreign body in the gastro-intestinal tract and a pyogenic abscess of the psoas muscle. James [16] reported the case of a child of 2½ years who was seen because of pain in the right thigh and flexion deformity of

15. Eitel, G. D.: Ingested Foreign Bodies in the Gastro-Intestinal Tract Requiring Surgical Removal, Minnesota Med. **18**:52-59 (June) 1935.

16. James, T. G. I.: Psoas Spasm Caused by a Foreign Body, Brit. J. Surg. **22**:622-623 (Jan.) 1935.

the right hip. A roentgenogram revealed a needle in the duodenum. At operation the needle was found to have perforated the posterior wall of the duodenum, with its point embedded in the substance of the psoas muscle. After removal of the foreign body, all symptoms disappeared. The fact that foreign bodies are not frequently found in so-called hematogenous abscess of the psoas muscle may be explained on the basis of the foreign body penetrating the substance of the psoas muscle with the introduction of infection, following which the foreign body may fall back into the lumen of the bowel and be passed. That a foreign body may penetrate the wall of the bowel, giving rise to the symptoms of localized or spreading peritonitis, then fall back into the lumen of the bowel and be passed, has been suggested by several authors. Ginzburg and Beller [14b] reported such a case in a youth of 19 years. At operation an acute perforation of the small intestine was found with an ulcer, the base of which contained multinuclear giant cells but in which no foreign body was found.

Foreign Bodies Causing Gastro-Intestinal Hemorrhage.—Hemorrhage from the gastro-intestinal tract resulting from the ulceration of an ingested foreign body is relatively infrequent. Only 1 such case has been seen at the Boston City Hospital.

Case 10.—A 27 year old man was transferred to the Boston City Hospital from the State Hospital for the Insane, where he had been treated for dementia praecox. He stated that for the past month or more he had been swallowing segments of bed springs. There were no symptoms referable to the gastro-intestinal tract until the day before transfer, when he began to suffer from severe abdominal pain and vomited a quantity of bright red blood. Physical examination revealed the abdomen to be rather distended, and a hard mass was felt in the epigastrium, which was flat to percussion. Roentgen examination revealed a large mass of metal in the stomach.

The day after transfer operation was performed through a high midline incision. The stomach was opened, and the following foreign bodies were removed: 132 segments of bed spring, 9 cut pieces of bed spring, 3 prune pits, a wad of tin foil and a piece of rubber from a motor tire. The wound in the wall of the stomach was closed with a double row of inverting sutures and the abdomen was closed around a drain.

Postoperatively, the patient was unmanageable. Despite restraints, he tore off the dressings repeatedly. The wound became septic, the sutures sloughed, the wound opened and a loop of intestine herniated through. The patient began to vomit and to show signs of peritonitis. His condition became progressively worse, and he died on the twelfth postoperative day.

Matthews [17] reported the case of a woman who had a fatal hemorrhage caused by ulceration due to a tiny bit of copper turning through the wall of the esophagus into the aorta. Wölfler and Lieblein [10]

17. Matthews, T. E.: An Obscure Case of Internal Hemorrhage, Brit. M. J. 1:111-112 (Jan. 18) 1930.

reported a case of fatal gastric hemorrhage from an ingested fish bone which had perforated the posterior wall of the stomach. Benda [18] found a fish bone in the superior mesenteric vein.

Foreign Bodies too Large to Pass Through the Gastro-Intestinal Tract.—Of the ingested foreign bodies which are too large to pass through the gastro-intestinal tract, the open safety pin presents a problem unto itself. The pin is usually swallowed by an infant or a young child, and often the activating motive behind the act is the poor example set by the mother in putting pins in the mouth while dressing the child. As stated previously, an open safety pin which passes always has the spring foremost. The pin which becomes impacted always has the open wedge, formed by the point and the head, foremost. A pin in such a position usually becomes impacted at the outlet of the stomach and in such a position frequently must be removed surgically. A case in point is the following:

CASE 11.—A. R., a 9 month old girl, was admitted to the hospital on July 9, 1931. The mother stated that thirty hours before admission the child had swallowed an open safety pin. She gagged slightly at the time but had been perfectly well since and was taking food and fluids normally. Physical examination gave negative results. The day of admission, while in the ward, the child vomited a small quantity of bright red blood. A roentgenogram of the abdomen on that day showed a large safety pin, open and with point downward, lodged in the pylorus. A second roentgenogram the following day showed no change in the position of the pin.

Operation was performed the day after the child's admission through a left upper rectus incision. The safety pin was palpated through the wall of the stomach. A ½ inch (1.3 cm.) incision was made in the anterior wall of the stomach, and the pin was removed. The wound in the gastric wall was closed, and the abdomen was closed in layers without drainage. Convalescence was entirely uneventful, and the patient was discharged from the hospital on the eleventh postoperative day.

There are several other methods of dealing with an open safety pin and other similar small foreign bodies in the stomach and the first portion of the duodenum. Five cases are reported [19] in which at lapa-

18. Benda, C.: Fremdkörper in der Vena meseraica superior, Berl. klin. Wchnschr. **47**:2110, 1910; cited by Bearse, C.: Fishbones as a Cause of Intestinal Perforation, New England J. Med. **201**:885-886 (Oct. 31) 1929.

19. (*a*) Greeley, Paul W.: Removal of Slender Foreign Bodies from the Stomach and Duodenum Without Gastrotomy or Duodenotomy, J. A. M. A. **101**: 119 (July 8) 1933. (*b*) Huff, W. B.: Removal of a Safety Pin from Stomach Without Gastrotomy, ibid. **94**:1655-1656 (May 24) 1930. (*c*) Monteith, W. B. R.: Removal of Foreign Body from Stomach of Infant, Brit. M. J. **1**:259 (Feb. 18) 1928. (*d*) Otten, Harry: Open Safety Pin in Stomach of Two Months Old Baby, J. A. M. A. **100**:736 (March 11) 1933. (*e*) Raymond, Sidney W.: Foreign Body in Duodenum: Report of Case and Method of Removal, ibid. **100**:337 (Feb. 4) 1933.

rotomy the pin was closed by palpation through the wall of the stomach. After closure it is "milked" into the end of a rubber tube, previously passed into the stomach, and the tube and pin are then withdrawn. This obviates the necessity for opening the stomach and should be attended with considerably less risk. A smaller safety pin in the stomach may be closed by palpation through the wall of the stomach and then allowed to pass on through the gastro-intestinal tract.

CASE 12.—V. M. S., a 3 year old girl, was admitted to the aural service on Oct. 4, 1934, with a history of having swallowed an open safety pin four hours previously. This had been attended with no untoward respiratory symptoms, and the results of the physical examination were entirely negative. Roentgen examination showed the pin to be lodged in the lower third of the esophagus with the point uppermost. After two unsuccessful attempts to remove the pin through the esophagoscope, the pin was pushed into the stomach. Further roentgen studies showed the pin to lie in the second portion of the duodenum, again with the point up, where it remained for the following week without showing a change of position on repeated roentgen examination.

Laparotomy was done on October 15 through an upper midline incision. The pin was easily located in the second portion of the duodenum. It was closed by palpation through the intestinal wall, after which the abdomen was closed without drainage.

After the operation the progress of the closed pin was followed through the intestinal canal by daily roentgenograms and was found in the stool on the fifth postoperative day. After an entirely uneventful convalescence the patient was discharged home on the fifteenth postoperative day.

The curves of the duodenum form an obstacle which often cannot be passed by an elongated foreign body, and nails, pins and other elongated objects must occasionally be removed by laparotomy. The following are cases in point:

CASE 13.—E. S., a 14 month old girl, was admitted to the hospital on March 25, 1918, with a history of having swallowed a nail 2 inches (5 cm.) long on the same day. There had been no systemic symptoms. Physical examination gave essentially negative results. A roentgenogram of the abdomen showed the nail, with point directed downward, in the right upper quadrant. The following day a small amount of a bismuth preparation was given by mouth, and a roentgenogram showed the nail to be lodged in the pylorus.

The child was observed in the ward for five weeks, during which time she continued to take food normally. Roentgenograms of the abdomen were taken at intervals of every four days, a total of ten being taken. At the end of the second week the nail had gone through the pylorus into the second portion of the duodenum, where it remained for the following three weeks without changing its position. At the end of this time laparotomy was done through an upper midline incision. The nail was located with some difficulty in the second portion of the duodenum. It was "milked" back into the first portion, where it was removed through a small stab incision in the wall of the bowel. The stab incision was closed with a purse-string suture, and the abdomen was closed in layers without drainage.

The child made an uneventful convalescence and was discharged on the twenty-first postoperative day.

CASE 14.—J. T., a 2 year old girl, was admitted to the hospital on Sept. 3, 1920, with a history of having swallowed a "stickpin," 3 inches (7.6 cm.) in length, twenty-four hours previously. There had been no subjective symptoms, and physical examination gave negative results. Fluoroscopic examination revealed the pin in the right upper quadrant. After six days' observation in the ward, further roentgen examination showed that the pin had not changed position. Operation was performed the following day through a right upper rectus incision. The pin was easily felt in the second portion of the duodenum. A small incision was made in the wall of the duodenum, and the pin was delivered through it. The incision in the intestine was closed with a double tier of catgut sutures, and the abdominal wall was closed without drainage.

Convalescence was complicated by scarlet fever, from which the child recovered after treatment in the contagion service. Slight superficial sepsis of the wound was easily controlled.

In dealing with an impacted foreign body one must keep constantly in mind the fact that there is a tendency for such an object to pass naturally, occasionally after long periods of remaining in the same location. It is necessary in all cases to make a roentgenogram of the abdomen immediately before operation to be certain of the location of the foreign body. By so doing, much operative trauma will be avoided, and an occasional patient will be spared the necessity of operation, as would have been the case in the following instance:

CASE 15.—J. G., an 11 year old school boy, was admitted to the hospital on Sept. 23, 1929, with a history of having swallowed a nail three weeks before. He was seen in the outpatient department the day of the accident, and roentgen examination at this time showed the nail to be in the stomach. One day later the nail was seen on roentgen examination to be lodged in the second portion of the duodenum. Frequent roentgenograms showed no progress of the foreign body, and the child was finally admitted to the hospital for operation, having suffered no untoward effects in the interval. Physical examination at the time of admission gave negative results. Further roentgenograms at the time of admission to the hospital and on the succeeding two days showed no progress of the foreign body. Operation was performed through a right rectus incision on the fourth day of hospitalization. The stomach and duodenum were carefully palpated, but no foreign body was felt. The ligament of Tritz was divided, and the entire duodenum was searched without success. Further exploration of the intestinal tract revealed the nail in the lower portion of the ileum, from which it was removed through a small incision in the wall of the bowel. Postoperative convalescence was uneventful.

Foreign Bodies Causing Obstruction to the Gastro-Intestinal Tract.—A foreign body which passes the esophagus ordinarily does not cause obstruction to the gastro-intestinal tract. Such an obstruction is usually due to multiple foreign bodies or to one of the several classes of bezoars. These usually cause symptoms of intermittent pyloric obstruction, with or without the presence of a palpable epigastric mass. In the case of a metal foreign body, the diagnosis is readily made by a simple roentgen-

ogram of the abdomen. In the case of a bezoar the diagnosis can usually be made with the aid of the meal of barium sulfate, although the bezoar may be confused with a polyp. Treatment consists in removal of the obstructing foreign body by gastrotomy.

The literature is replete with remarkable examples of the number and kinds of foreign bodies removed from the stomach at gastrotomy. Hildreth and Casey [20] reported a case in which 48 teaspoons together with other assorted bits of hardware were removed from the stomach by gastrotomy. Kennedy [21] removed 500 pieces of small metal objects from the stomach of an insane person, while Chalk and Foucar [22] reported a remarkable case in which no less than 2,533 foreign bodies were similarly removed. In the latter case there was an epigastric mass measuring 4 inches (10 cm.) in diameter, which was made up of pins, pieces of wire and other small bits of metal. This is the largest number of foreign bodies ever removed from the stomach at operation.

It is significant that multiple foreign bodies are usually found in insane persons, who swallow them with suicidal intent. All insane patients exhibiting unusual abdominal symptoms should be submitted to roentgen examination.

Bezoars are characterized by the gradual accumulation, usually in the stomach, of ingested material, which may be from several sources. They have been known since ancient times, when they were highly prized as antidotes for poisons. Bezoars may accumulate from the repeated ingestion of hair (trichobezoar), string, vegetable fiber (phytobezoar), such as persimmon, pumpkin, celery, etc., and from chemicals, such as bismuth, salol and shellac. Swain's case in which a trichobezoar weighing 5 pounds and 3 ounces was removed from the stomach has been alluded to previously. Kortman [23] reported a case in which 2 shellac stones weighing 670 Gm. remained in the stomach for sixteen years.

MANAGEMENT OF THE INDIVIDUAL CASE OF INGESTED FOREIGN BODY

Diagnosis.—The diagnosis of an ingested foreign body can usually be made from the history. This, of course, is not true of infants and young children, whose history may be misleading. In the absence of perforation, physical examination usually gives negative results. Exam-

20. Hildreth, E. Raymond, and Casey, Robert B.: Foreign Bodies in Stomach, J. A. M. A. **102**:604 (Feb. 24) 1934.

21. Kennedy, R. Stewart: Five Hundred Foreign Bodies in the Stomach, Brit. M. J. **1**:1262-1264 (June 22) 1935.

22. Chalk, S. G., and Foucar, H. O.: Foreign Bodies in the Stomach, Arch. Surg. **16**:494-500 (Feb.) 1928.

23. Kortman, cited by Friedenwald and Rosenthal.[4]

ination of the abdomen should be done with great care in order to form a basis for comparison with subsequent examinations. Should abdominal tenderness develop in a patient who has swallowed a foreign body, particularly if the foreign body is pointed at one or both ends, laparotomy should be performed at once.

In the case of a radiopaque foreign body roentgen examination is of the greatest importance and should include not only anteroposterior but lateral views as well. In this way it is usually possible to determine the location of the foreign body in the gastro-intestinal tube. In this respect it is interesting to note the ingenuity displayed by clinicians before the days of the x-ray. Cant [24] reported the case of a woman who was said to have swallowed a razor. The patient was given 20 minims (1.2 cc.) of dilute hydrochloric acid. After one hour the contents of the stomach were aspirated, and the washings were filtered, evaporated and redissolved. The presence of iron in large quantities was demonstrated by means of the prussian blue test.

The preoperative diagnosis of acute or chronic perforation of the gastro-intestinal tract by a foreign body will seldom be made in the absence of a definite history of ingestion of a foreign body. It should be suspected in cases of peritonitis in which the etiology is atypical. When the suspected pathologic process is not found at operation, it is important to explore the infected region with perforation by a foreign body in mind, so that the etiologic factors may be adequately dealt with.

Treatment.—Treatment for an ingested foreign body in the absence of perforation should always be conservative, until it is definitely shown that the foreign body will not pass naturally or until it is evident that there is, or is about to be, perforation. Careful daily examinations of the abdomen should be made. With the development of abdominal tenderness, laparotomy should be performed without delay. Daily roentgenograms of the abdomen, both anteroposterior and lateral, should be made so that the progress of the foreign body through the gastro-intestinal tract can be watched. It has been shown previously that foreign bodies which pass the gastro-intestinal tract usually do so within seven days from the time of ingestion. Surgical intervention should therefore be considered seriously in the case in which the foreign body remains in one place in relation to the viscerae (not necessarily in relation to the bony landmarks) for seven days or more. It is also important that stools be strained to confirm the passage of the foreign body through the gastro-intestinal tract.

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24. Cant, W. J.: Case of Swallowing a Razor; Gastrotomy; Death, Lancet **1**:20-21, 1893.

TABLE 5.—*Cases from Literature in Which a Foreign Body Has Perforated the Gastro-Intestinal Tract and in Which Site of Perforation Was Definitely Established*

Author	Foreign Body	Site of Perforation	Type of Injury to Gastro-Intestinal Tract	Symptoms and Signs	Preoperative Diagnosis, When Stated	Operation and Findings	Result
Bacon, T. S., and Corliss, P. G.: New England J. Med. **204**: 214-215 (Jan. 29) 1931	Fish bone ¾ inch long	Sigmoid flexure	Abscess formation	Swelling for about 4 wk.; signs of encapsulated fluid	Ovarian cyst	No operation	Died of pneumonia
Black, J. M.: Brit. M. J. **2**: 1198 (Dec. 28) 1929	Wire 2 inches long	Loop of ileum	Chronic penetration	Intermittent pain in right lower quadrant for 3 mo.	Acute appendicitis	Omentum around site of perforation; wire and omentum removed; perforation closed; appendectomy	Recovery
Cannaday, J. E.: Ann. Surg. **94**: 218-232, 1931	Nail, 10 penny	Cecum	.....	Not stated	Correct	.....	Recovery
Douglas, J.: J. A. M. A. **95**: 265-266 (July 26) 1930	Fish bone	Pylorus	Abscess formation	Pain and tenderness in right upper quadrant with fever, leukocytosis and mass in right hypochondrium	Acute cholecystitis	Perforation of pylorus and penetration of wall of duodenum opposite; abscess under liver and penetration of liver by bone; drainage of abscess	Recovery
Durman, D. C., and Belz, F.: J. A. M. A. **94**: 1830 (June 7) 1930	Tooth pick	Sigmoid flexure	Abscess formation	Dull aching pain for 6 mo. in left lower quadrant; tumor 12 cm. in diameter in left lower quadrant	.....	Drainage of abscess	Recovery
Eitel [15]	Medicine dropper	Duodenum, junction of 2d and 3d portions	Acute perforation	Sudden pain (?); present some time	Correct	.....	Recovery
Friedenwald and Rosenthal [4]							
McKee (1879), cited by Friedenwald and Rosenthal [4]	Copper wire 3 inches long	Stomach	Abscess formation	Acute pain in right lower quadrant with tumor	.....	Abscess cavity opened; wire removed; drainage	Recovery
Gerard (1883), cited by Friedenwald and Rosenthal [4]	Wood stick 21.5 cm. long	Stomach	Abscess formation	Abdominal pain, nausea and vomiting; palpable tumor	.....	Abscess opened; 10 cm. of foreign body removed; castor oil given and remainder of foreign body passed per via naturales	Recovery
Fricker (1897), cited by Friedenwald and Rosenthal [4]	Crocheting needle	Stomach	Abscess formation	Anorexia; abdominal pain; emaciation for 3 mo.; abscess of entire left side of abdomen	.....	Incision and drainage of abscess; crocheting needle removed; second incision and removal of multiple foreign bodies from stomach	Recovery
Mikulicz (1901), cited by Friedenwald and Rosenthal [4]	Artificial teeth	Stomach (posterior wall)	Chronic penetration	Present in stomach 6 mo.	Correct (roentgenography)	Teeth removed through gastrotomy opening in anterior wall	Recovery

Mathis* (1602), cited by Friedenwald and Rosenthal [4]	Knife 21 cm. long	Stomach (pylorus)	Chronic penetration (?)	Present in stomach 51 days	.....	Application of plasters to abdomen; penetration of pylorus by knife; removal of knife	Recovery
Wessner (1692), cited by Friedenwald and Rosenthal [4]	Knife	Stomach	Abscess formation	Abscess of abdominal wall 7 mo. after ingestion of foreign body	.....	Drainage of abscess; knife presented in wound; knife removed	Recovery
Huebner (1720), cited by Friedenwald and Rosenthal [4]	Knife 16.5 cm. long	Stomach	Abscess formation	Acute abdominal pain 3 days after swallowing foreign body	.....	Drainage of abscess of left side of hypochondrium; knife presented in wound on eleventh day; removal of knife	Recovery
Frisac (1786), cited by Friedenwald and Rosenthal [4]	Knife 4.5 cm. long	Stomach	Chronic penetration (?)	Present in stomach 11 days	.....	Epigastric incision; penetration of wall of stomach by knife; removal of knife	Recovery
Fidelli (1836), cited by Friedenwald and Rosenthal [4]	Brass fork and 4 pronged fork without handle 10 cm. long	Stomach	Abscess formation	Present 2½ yr.; abscess of right side of hypochondrium after 15 mo.; drainage of abscess for 11 mo. later; removal of foreign bodies	.....	Drainage of abscess and removal of foreign bodies	Recovery
Holbeck* (1858), cited by Friedenwald and Rosenthal [4]	Fork 21 cm. long	Stomach	Abscess formation	Nausea, anorexia, vomiting; abscess of abdominal wall	.....	Drainage of abscess; foreign bodies extracted	Died 3 mo. later of caries of sternum and ribs
Czerny (1895), cited by Friedenwald and Rosenthal [4]	Needle	Stomach	Acute perforation	Abdominal pain for 8 days; epigastric tenderness	.....	Induration at point of perforation; no adhesions	Recovery
Hashimoto (1889), cited by Friedenwald and Rosenthal [4]	Tooth brush	Stomach (anterior wall)	Abscess formation	Object in stomach 7 days	.....	Perforation of anterior wall of stomach; point of perforation excised and resutured after removal of foreign body; peritonitis present	Died of peritonitis
Halliwell (1899), cited by Friedenwald and Rosenthal [4]	Hat pin	Stomach (posterior wall)	Acute perforation	Pain in left iliac fossa and tenderness over descending colon	.....	Colon normal; needle in stomach with point embedded in posterior wall; point pushed through stomach and omentum and head passed by rectum	Recovery
Inch (1902), cited by Friedenwald and Rosenthal [4]	Nails, pins, needles and buttonhook (12 articles)	Stomach	Chronic penetration (?)	Abdominal pain and distress	.....	Perforation of stomach by pin; stomach opened and emptied; foreign bodies removed from ileum	Recovery
Gaither, E. H.: M. Clin. North America **16**: 1185-1197, 1933	Prune seed	Ileum	Acute perforation	Recurrent pain in lower part of abdomen for 1 mo.; sudden severe pain in lower part of abdomen	Acute appendicitis	Prune seed free in abdominal cavity; resection of 30 cm. of ileum and side to side anastomosis	Recovery

TABLE 5.—*Cases from Literature in Which a Foreign Body Has Perforated the Gastro-Intestinal Tract and in Which the Site of Perforation Was Definitely Established—Continued*

Author	Foreign Body	Site of Perforation	Type of Injury to Gastro-Intestinal Tract	Symptoms and Signs	Preoperative Diagnosis, When Stated	Operation and Findings	Result
Ginzburg and Beller [14b]	Chicken bone	Ileum	Acute perforation	Colicky pain for a few weeks; worse for 3 days; signs of peritonitis	Acute appendicitis	Extraction of foreign body; closure of perforation	Recovery
	Fish bone	Hepatic flexure	Abscess formation	Epigastric pain and pain in right upper quadrant with nausea; mass in right upper quadrant	Pericholecystic abscess	Abscess extending down to hepatic flexure and containing foreign body; drainage	Recovery
	Toothpick	Cecum (posterior wall)	Abscess formation	Pain in right lower quadrant for 5 days; mass palpable	Abscess of appendix	Retrocecal abscess containing fragment of tooth pick; drainage	Recovery
	Fish bone	Splenic flexure	Abscess formation	Pain in left upper quadrant for 8 wk.; mass in left lower quadrant; barium enema negative	.....	Drainage of abscess due to 2 fish bones perforating the splenic flexure	Recovery
	Chicken bone	Small intestine in umbilical hernia	Abscess formation	Umbilical hernia with abscess	.....	Abscess due to 2 pieces of chicken bone perforating the small bowel	Recovery
	Chicken bone	Terminal portion of ileum in umbilical hernia	Abscess formation	Umbilical hernia with abscess	.....	Abscess contained chicken bone; bone perforated lower portion of ileum	Died
Hawkyard, A., and Armitage, G.: Brit. M. J. **1**: 577-578, 1931	Rabbit's rib	Sigmoid flexure	Acute perforation	Acute abdominal pain of 20 hours' duration	Acute appendicitis	Removal of foreign body; closure of perforation; incidental appendectomy; drainage	Recovery
Henderson and Gaston	Chicken bone	Stomach	Acute perforation	Pain in right side of hypochondrium for 6 days; severe for 60 hr.	Acute cholecystitis	Extraction of foreign body; closure of defect; cholecystectomy; drainage	Recovery
	Dried thyme (wood)	Probably duodenum	Chronic perforation	Epigastric pain for 24 hr.	Perforated peptic ulcer	Omentum adherent to anterior wall of pylorus and first portion of duodenum; foreign body free in peritoneal cavity; no defect found to close; drainage	Recovery
	Common pin	Cecum	Abscess formation	Pain in right lower quadrant for 3 wk.; palpable, tender mass	Appendical abscess	Drainage of abscess	Recovery

	Common pin	Descending colon	Chronic perforation	Pain in left lower quadrant for 1 mo.; pin swallowed 2 days before onset of symptoms; tender throughout left side of abdomen	Correct (roentgenographic)	Extraction of pin; closure of defect in colon and of defect where pin had perforated a loop of ileum; drainage	Recovery
	Open safety pin	Duodenojejunal flexure	Acute perforation	7 mo. infant; pin swallowed 12 days before operation; no progress by roentgen examination	Correct (roentgenographic)	Extraction; closure of defect; drainage	Died
	Wood splinter	Small intestine	Acute perforation	Pain in right lower quadrant for 24 hr.; tenderness in right lower quadrant	Acute appendicitis	Closure of defect after removal of foreign body; incidental appendectomy; drainage	Recovery
	Pieces of bed spring	Cecum	Acute perforation	Abdominal pain and tenderness	Correct (roentgenographic)	Perforation of cecum; removal of 6 pieces of bed spring from cecum; 4 from sigmoid flexure with lead pencil and 4 matches; no perforation of sigmoid flexure	Died
	Wood splinter	Transverse colon	Acute perforation	Pain in right lower quadrant for 7 days; tenderness and spasm in right lower quadrant	Acute appendicitis	Incidental appendectomy; closure of defect after removal of foreign body	Recovery
	Squash rind	Ileum	Acute perforation	Abdominal pain for 7 hr.	Acute appendicitis	Foreign body removed; defect closed; drainage	Recovery
Herbst, R. H., and Miller, E. M.: J. A. M. A. **106**: 2125-2128 (June 20) 1936	Chicken bone	Sigmoid flexure (diverticulum)	Chronic perforation	Vesicocolonic fistula	.....	Four stage operation	Recovery
James [16].....	Needle	Duodenum (posterior wall of first portion)	Acute perforation	Pain in upper part of right thigh and flexion deformity of hip	Correct	Needle penetrated into psoas muscle; removal; closure of defect	Recovery
Little, Y. A.: J. A. M. A. **62**: 929-930 (March 21) 1914	Lead pencil	Stomach	Chronic penetration	Intense abdominal pain with spasm; white cell count 25,000	.....	Removal of pencil; closure of defect; drainage	Recovery
Lupton, W. J. E.: Lancet **2**: 1179-1180 (Dec. 3) 1927	Wire 2 inches long	Stomach (pyloric end)	Chronic penetration	Pain for 4 days in right side of abdomen	Acute appendicitis	Wire perforated into large omental mass; removal of wire; drainage; died of peritonitis	Died
Macewen, J. A. G.: Lancet **2**: 785, 1919	Common pin	Cecum (near base of appendix)	Acute perforation	Abdominal pain for 1 wk. with signs of general peritonitis	Acute appendicitis	Died 1 hr. after operation	Died
Maxeiner, S. R., in discussion on Eitel,[15] p. 581	Tooth pick	Sigmoid flexure (diverticulum)	Abscess formation	.....	.....	Drainage of abscess	Recovery
	Campaign button	Sigmoid flexure (malignancy of)	Abscess formation	.....	.....	Drainage of abscess	Recovery

TABLE 5.—*Cases from Literature in Which a Foreign Body Has Perforated the Gastro-Intestinal Tract and in Which the Site of Perforation Was Definitely Established—Continued*

Author	Foreign Body	Site of Perforation	Type of Injury to Gastro-Intestinal Tract	Symptoms and Signs	Preoperative Diagnosis, When Stated	Operation and Findings	Result
McClintic, B. S.: Mil. Surgeon **75**: 75-78, 1934	Tooth pick	Cecum	Acute perforation	Acute abdominal symptoms resembling appendicitis	Acute appendicitis	.....	Recovery
McLanahan, S.: J. A. M. A. **95**: 1424 (Nov. 8) 1930	Tooth pick	Cecum	Abscess formation	Symptoms of acute appendicitis of 24 hours' duration	Acute appendicitis	Tiny perforation of lateral wall of cecum by tooth pick with small abscess; closure of perforation; drainage	Recovery
Norinder, E.: Acta chir. Scandinav. **76**: 136-146, 1935	Fish bone	Stomach	Abscess formation	Pain in loins; chills, fever, anorexia and emaciation; light stools; dark urine	Cholecystitis; suppurative cholangitis; pneumonia	No operation; postmortem examination; abscess of liver from perforations of lesser curvature by fish bone; abscess ruptured through right side of diaphragm to cause encapsulated empyema of right side of chest	Died
Pike, J. B.: Brit. M. J. **2**: 413, 1919	Nail	Cecum	Chronic penetration (?)	Pain in right lower quadrant with tenderness and muscle spasm	Acute appendicitis	Nail removed; defect closed	Recovery
Rivers, A. B., and Davison, H. L.: Ann. Int. Med. **4**: 742-751, 1931	Tooth pick	Duodenum, 1st portion	Chronic penetration	Recurrent attacks of pain in right upper quadrant for 2 yr.	.....	Tooth pick sealed off by adhesions	?
	Squash rind	Stomach	Acute perforation	Epigastric pain and hematemesis	.....	No operation; autopsy; perforation of stomach; fatal peritonitis	Died
Schilling, H.: Acta chir. Scandinav. **74**: 455-456, 1934	Open safety pin 5 cm. long	Duodenum					
	Piece of metal	Cecum	Abscess formation	.....	.....	Retroperitoneal abscess drained	
Shallow, T. A.: S. Clin. North America **14**: 57-76, 1934	Needle	Jejunum	Chronic penetration	.....	.....	Needle also peneterated adjacent loop of ileum; removal of needle; drainage; perforations not closed	Recovery
	Needle	Duodenum, 3d portion	Chronic penetration				
	Bobette pin	Duodenum, 3d portion	Chronic penetration	.....	.....	Pin also eroded through transverse colon, causing duodenocolic fistula; removal of foreign body and repair of fistula	Recovery ?

	Open safety pin	Cecum	Abscess formation	Pain in right upper quadrant	.....	Local peritonitis present	
Sivertsen, I., in discussion on Eitel [15]	Bits of screen wire	Small bowel	Acute perforation	.....	.....	Resection	Recovery
Stone and Owings [14c]	Fish bone	Stomach	Chronic penetration	Epigastric pain for 6 mo.; palpable epigastric mass	.....	Resection of portion of stomach together with adherent omentum; fish bone found in sectioning specimen	Recovery
Tuft, L.: M. J. & Rec. **119**: 30, 1924	500 straight pins	Stomach	Chronic penetration	Pins swallowed with suicidal intent 7 wk. before operation	.....	Large perforation of stomach with local peritonitis; pins removed	Died
Vestal, P. W.: New England J. Med. **203**: 1190-1200, 1930	Tooth pick	Cecum	Abscess formation	Three days of symptoms simulating acute appendicitis	Acute appendicitis	Perforation of anterolateral aspect of cecum opposite ileocecal valve; removal of foreign body; closure of defect; drainage	Recovery
Wallace, J. T.: Am. J. Surg. **19**: 453-455, 1933	Open safety pin	Duodenum, 2d portion	Chronic penetration	Pin remained stationary for 7 days	.....	Point of pin just under serosa, covered by adherent omentum; removal of pin; closure of defect	Recovery
Wheeler, P. H.: New England J. Med. **214**: 830-832, 1936	Multiple tacks, staples, etc.	Stomach, lesser curvature	Chronic penetration	Vomiting of blood and coffee-ground material for several months	Correct (roentgenographic)	Excision of perforated ulcer caused by foreign bodies; removal of foreign bodies	Recovery
Wölfler and Lieblein [10]							
Schwabe	.....	Stomach					
Soyka-Chiari	.....	Duodenum					
Winge	.....	Ileum portion of terminal					
von Kranzle	.....	Duodenum					
Diemerbrock	.....	Small intestine	Acute perforation				
Dehner	Wire	Ileum	Abscess formation				
Menzel	Lint	Transverse colon	Abscess formation				
Brevitt	Pencil	Ascending colon	Chronic penetration (?)				
Gemmel	Nail	Stomach	Acute perforation (?)				

Various types of diets have been recommended [25] in the hope that by feeding coarse food the vegetable fibers will become enmeshed in the foreign body and aid its passage. Jackson,[7] however, stated that a diet that is in all respects the usual diet should be given, and he warned in particular against the use of catharsis.

In certain instances, manipulation under the fluoroscope may be of assistance in dislodging an impacted foreign body and allowing it to resume its passage through the gastro-intestinal tract.[26] Dudko and Brailowski [27] described the case of a 15 year old girl who swallowed a small nail, which became lodged in the duodenum. A duodenal tube was passed under roentgen control, and air was blown into the duodenum through the tube. During this procedure the nail dislodged itself and was passed by rectum four days later.

The operative treatment for an ingested foreign body has, in large part, been dealt with previously. To recapitulate, in the case of perforation the foreign body should be removed and the site of perforation closed. Whether or not the peritoneal cavity should be drained will depend on the site of perforation and the degree of contamination of the peritoneal cavity. In the case of an impacted foreign body it is probably better, in general, to remove the foreign body through a small incision in the wall of the bowel. In the case of a small open safety pin impacted in the intestine, it may be advisable simply to close the pin by palpation through the intestinal wall, allowing it to progress through the gastro-intestinal tract without danger of impaction or perforation.

A patient with an open safety pin in the stomach may often be adequately treated without opening the stomach at laparotomy by closing the pin by palpation through the wall of the stomach and then "milking" it into the end of a tube previously passed into the stomach. Withdrawal of the tube delivers the foreign body without danger of contamination to the peritoneal cavity.

A foreign body in the terminal portion of the ileum or the ascending colon may be "milked" into the lumen of the appendix and removed with the appendix.[28]

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25. Sauer, L. W.: Dr. Boot's Nonsurgical Treatment for Swallowed Foreign Bodies, J. A. M. A. **98**:1981 (June 4) 1932. Vinson and Deissler.[11a]

26. (*a*) Scott, S. G.: Method of Dealing with Swallowed Object, Brit. M. J. **1**:133 (Jan. 28) 1928. (*b*) Strangl, F. H.: Intestinal Foreign Bodies, Minnesota Med. **13**:909-910 (Dec.) 1930.

27. Dudko, M. O., and Brailowski, B. S.: Removal of Foreign Bodies from Duodenum with Aid of Duodenal Sound, Zentralbl. f. Chir. **57**:1476-1478 (June 14) 1930; cited by Greeley.[10a]

28. Chaton, M.: Brooch Swallowed by Infant Eleven Months Old, Localized in Cecal Inguino-Scrotal Hernia and Extracted by Appendectomy, Mém. Acad. de chir. **62**:236-238 (Feb. 19) 1936. Nutting, George K.: Appendectomy for Swallowed Clinical Thermometer, J. A. M. A. **100**:572 (Feb. 25) 1933. Strangl.[26b]

SUMMARY AND CONCLUSIONS

1. Foreign bodies swallowed by infants and young children are usually the result of carelessness on the part of parents. Dentures covering a large part of the sensitive area of the mouth are frequently responsible for an adult unwittingly swallowing a foreign body.

2. An ingested foreign body that passes per vias naturales usually does so within seven days, regardless of the age of the patient or the type of the foreign body.

3. An ingested foreign body that perforates the gastro-intestinal tract may do so at any point along the tract. Statistically, the stomach seems to be perforated about twice as frequently as is any other portion.

4. Acute perforation of the gastro-intestinal tract by an ingested foreign body is most likely to occur in the small intestine or cecum. Chronic perforation and abscess formation are more likely to occur in the stomach and colon. Cases seen at the Boston City Hospital are presented illustrating the various types of perforation.

5. It is suggested that a foreign body perforating the gastro-intestinal tract and becoming embedded in the substance of the psoas muscle may occasionally be responsible for pyogenic abscess of the muscle.

6. Hemorrhage from the gastro-intestinal tract caused by an ingested foreign body is unusual. One such case seen at the Boston City Hospital is presented.

7. The problem of the ingested open safety pin is discussed.

8. The curves of the duodenum are a frequent site of impaction of elongated foreign bodies. Surgical intervention for an impacted foreign body should always be immediately preceded by roentgen examination to determine whether or not the foreign body has changed position in the twenty-four hours preceding operation.

9. A discussion of the indications for, and the essential details of, the conservative and surgical treatment for an ingested foreign body is given.

HISTOLOGIC STRUCTURE OF THE NORMAL THYROID GLAND

VARIATIONS AND THEIR SIGNIFICANCE IN THE INTERPRETATION OF PATHOLOGIC CONDITIONS OF THE THYROID GLAND

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Diseases of the thyroid gland, particularly the hyperthyroid states, have caused so much confusion among clinicians and pathologists that it is often difficult to place in the same classification identical diseases of this gland with different nomenclature. It is improbable that the great number of terms which can be found in the literature to designate the various diseases of the thyroid gland actually represents such a variety of diseases. This extensive terminology no doubt suggests the multiplicity of interpretations which have been made by those who are concerned with diseases of the thyroid gland.

In order to understand the diseased thyroid, it is important to have a clear concept of the variations which may occur in the normal gland during a life span.

An examination of some of the textbooks dealing with histology, pathology and diseases of the thyroid reveals that the normal thyroid organ is a gland situated in the neck, composed largely of acini lined by cuboidal cells; that these acini may vary in size, depending on age and locality, and that the normal weight of the gland is about 32 Gm.

Hertzler [1] stated that the histologic structure of the thyroid gland will be found to be fairly constant if the various changes occurring at different stages during life are taken into consideration.

McCarrison [2] likewise recognized the variable changes which occur in the normal thyroid gland as a result of age and locality. The changes which he observed were particularly those which had reference to the size of the acini and the amount of interacinar epithelium and interlobular stroma. He did not mention the development of nodules in an otherwise normal gland.

The life cycle of the thyroid gland has been studied by European authors and seems to have been fairly well established, particularly in

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From the Department of Surgery of the University of Minnesota.

1. Hertzler, A. E.: Diseases of the Thyroid Gland, ed. 2, St. Louis, C. V. Mosby Company, 1929.

2. McCarrison, Robert: Etiology of Endemic Goiter, Lancet **1**:147-154, 219-226 and 365-373, 1913.

Germany and Switzerland. Wegelin,[3] Hesselberg,[4] Zelinska,[5] Kloeppel,[6] Isenschmid,[7] Sanderson,[8] Schaer[9] and Clerc[10] are the principal ones from whom these data can be obtained.

Alexander Hellwig[11] seems to have obtained a clear idea of the variabilities in the structure of the thyroid gland in North America. He pointed out that the acini and the incidence of nodules may vary in size and percentage, respectively, depending on age and locality.

In a previous study of the life cycle of the thyroid gland from Minnesota it has been shown that there may be numerous variations in the gross and the histologic structure of the normal gland.

MATERIAL AND METHOD OF INVESTIGATION

This paper deals with the same material as that which was used in a previous paper.[12] Five hundred thyroid glands were examined grossly and histologically. These glands were taken from persons who died of diseases in which the thyroid gland played no part and who were not accredited with a goiter during their routine physical examination made at the time of their admission to the hospital. Large glands or glands which were found to contain nodules were not excluded from the series unless the presence of a "goiter" had been noted on routine physical examination.

All glands were serially sectioned for gross examination, and histologic sections were made from representative areas. The percentage incidence of nodules was determined. The acini were measured with a micrometer, and the size and shape

3. Wegelin, C.: Die Schilddrüse, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 8.

4. Hesselberg, Cora: Die menschliche Schilddrüse in der foetalen Periode und in den ersten sechs Lebensmonaten, Frankfurt. Ztschr. f. Path. **5**:322-350, 1910.

5. Zelinska, Marie: Beitrag zur Kenntnis der normalen und strumösen Schilddrüse des Menschen und des Hundes, Virchows Arch. f. path. Anat. **136**: 170-194, 1894.

6. Kloeppel, Franz C.: Vergleichende Untersuchungen über Gebirgsland- und Tieflandschilddrüsen, Beitr. z. path. Anat. u. z. allg. Path. **49**:579-593, 1910.

7. Isenschmid, Robert: Zur Kenntnis der menschlichen Schilddrüse im Kindesalter, Frankfurt. Ztschr. f. Path. **5**:205-254, 1910.

8. Sanderson, Elizabeth: Die Schilddrüsen vom 15-25 Lebensjahr, aus der Norddeutschen Ebene und Küstengegend sowie aus Bern, Frankfurt. Ztschr. f. Path. **6**:312-334, 1911.

9. Schaer, Hans.: Vergleichende Untersuchungen an Schilddrüsen zwischen dem 25 und 50 Lebensjahr, Frankfurt. Ztschr. f. Path. **36**:249-274, 1928.

10. Clerc, Edward: Die Schilddrüse im hohen Alter. Vom 50. Lebensjahr an, aus der norddeutschen Ebene und Küstengegend sowie aus Bern, Frankfurt. Ztschr. f. Path. **10**:1-19, 1922.

11. Hellwig, C. Alexander: Geographic Pathology of Goiter, Surg., Gynec. & Obst. **55**:35-44, 1932; Die Lebenskurve der nordamerikanischen Schilddrüse, Endokrinologie **5**:323-336, 1933.

12. Rice, Carl O.: Life Cycle of the Thyroid Gland in Minnesota, West. J. Surg. **39**:925-940, 1931.

of the acinar epithelium were determined. The quantity of interacinar epithelium and interlobular stroma in relation to the other structures was estimated. Some of these factors have been dealt with more in detail in a previous paper.

The present paper endeavors to demonstrate photographically the histologic variations which occur. It also aims to correlate these findings and to establish their significance in the interpretation of the most frequently encountered disease of the thyroid gland.

In addition, this paper includes the results of the gross and histologic examinations of 121 goiters which were diagnosed clinically as toxic adenoma. Among these, there were 10 from persons who were found to have exophthalmos on physical examination. These 10 growths served as the basis on which the final histologic differentiation between exophthalmic goiter and toxic adenoma was made.

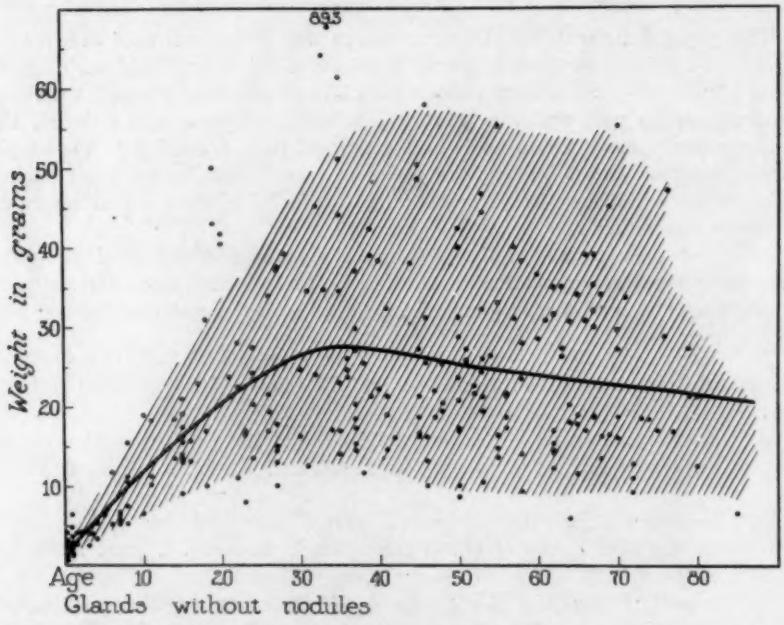

Fig. 1.—Curve showing the weight of thyroid glands in Minnesota during a life span. The dots indicate the weight of the individual glands; the black line indicates the average weight through the various ages, and the shaded area represents the range of variability.

RESULT OF INVESTIGATION OF WEIGHT

These studies have shown that the weight of the thyroid gland at birth averages 1.5 Gm. As the child grows older the weight of the gland increases rapidly. It reaches its maximum, averaging about 30 Gm. in early adult life. After that, it decreases gradually to the end of the life span. The range of normal variability in the weight of the adult gland was found to be from 10 to 50 Gm. (fig. 1). It therefore should not necessarily be claimed, as may frequently be heard at autopsy, that a

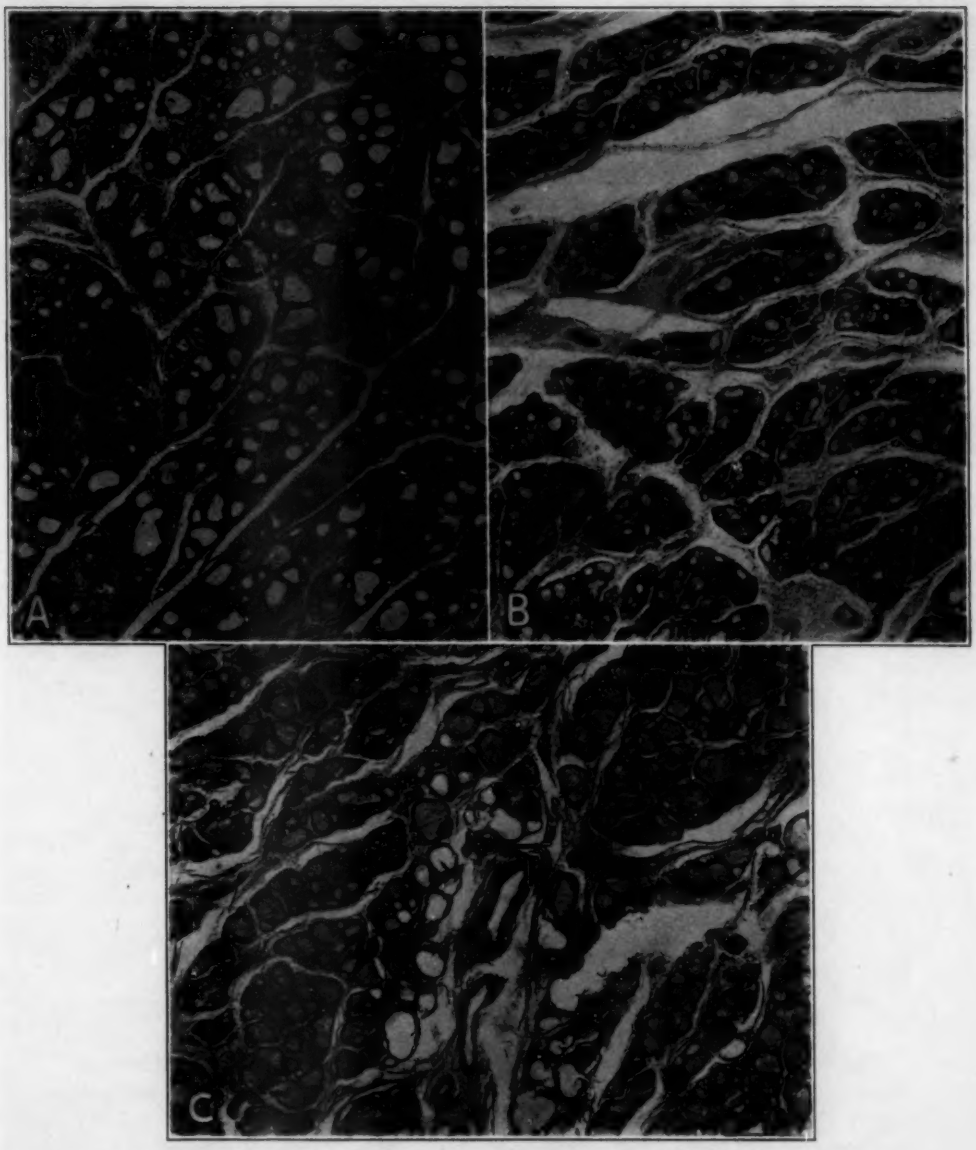

Fig. 2.—*A*, a section from the thyroid gland of a stillborn infant. The gland weighed 1.7 Gm., and the acini measured 84 microns in diameter. The interlobular septums are distinct, there is no colloid and there are many interacinar epithelial cells. Magnification, × 174. (All photomicrographs are of the same magnification, except figure 4 *C*, which was erroneously photographed at a magnification of 250 ×.) *B*, a section from the thyroid gland of a 3 month old infant. The gland weighed 2.3 Gm., and the acini measured 62 microns in diameter. There is an abundance of interlobular fibrous tissue, the colloid is beginning to appear and the interacinar epithelial cells are less abundant than in *A*. C, a section from the thyroid gland of a 6 month old child. The gland weighed 2.2 Gm., and the acini measured 134 microns in diameter. The interlobular septums are still distinct, the colloid occupies most of the acini and there is little interacinar epithelium.

gland weighing 40 or 50 Gm. is goitrous. A gland of this size found in a person at puberty or earlier in all probability is goitrous, but if it is found in an adult it cannot be called goitrous on this basis alone, because the normal range of variability in weight will allow it to remain within normal limits. Histologic examination of those glands which weighed more than 45 Gm. did not reveal any changes significant of goiter and showed no essential difference in their histologic structure from those which weighed less than 45 Gm. There was no evidence of increased *Polster* formation or epithelial proliferation whereby these heavier glands could be classified as colloid goiters, nor were their acini any larger than those of the lighter glands.

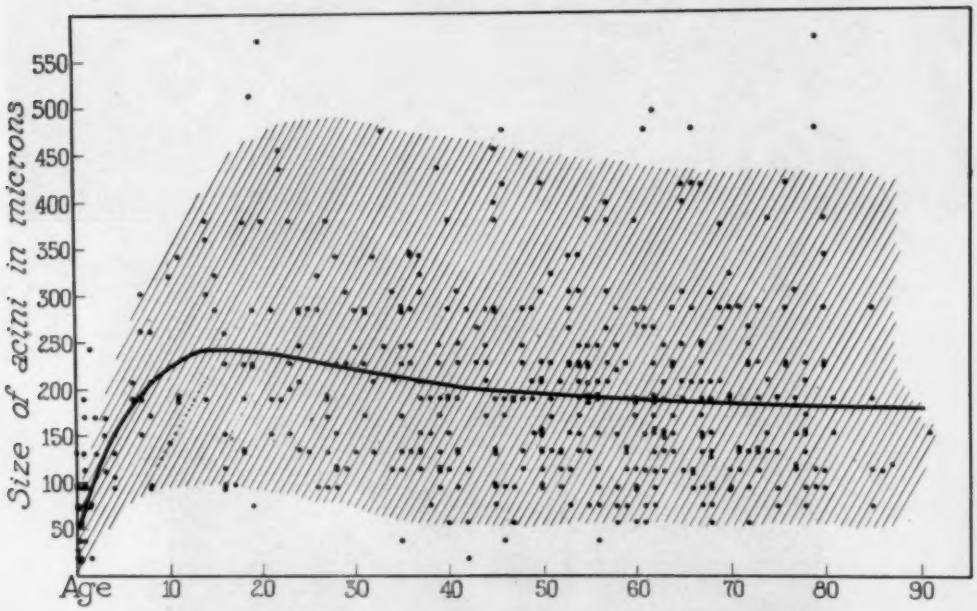

Fig. 3.—Curve showing the size of the acini in thyroid glands from Minnesota during a life span. The dots represent the average size of the acini in each individual gland; the black line indicates the average size of the acini through the various ages, and the shaded area represents the range of normal variability.

ACINI

In conjunction with this change in the weight of the gland there is also a change in the size of the acini. At infancy the acini are small and contain little or no colloid (fig. 2). As a person becomes older, the acini increase in size, reaching their maximum in early adult life. Following this there is again a decrease in the size of the acini, which progresses to old age (fig. 3; compare figs. 2*A* and 6*A*). Not infrequently the acini of the senile thyroid gland resemble those of the infantile gland,

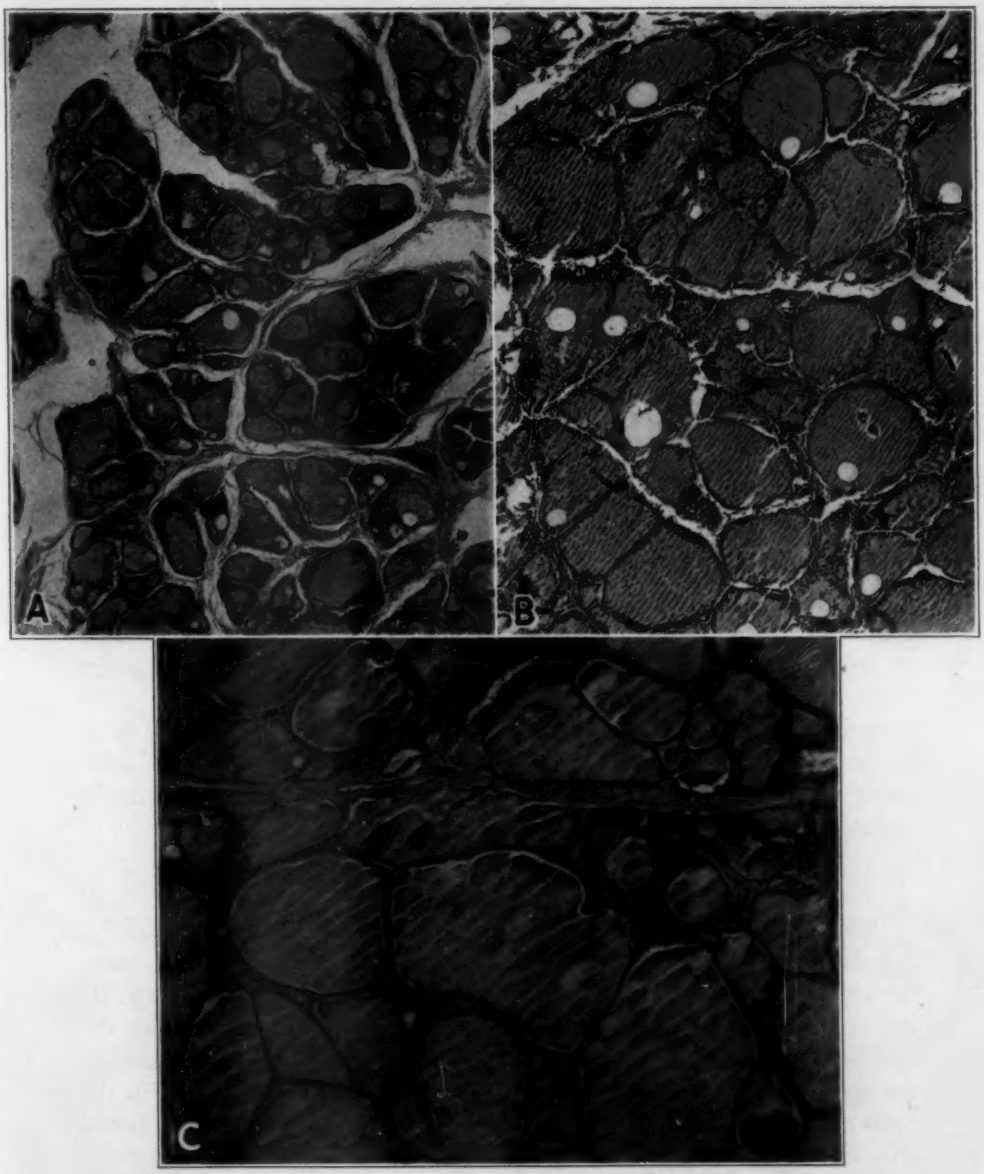

Fig. 4.—*A*, a section from the thyroid gland of a 7 year old child. The gland weighed 5.1 Gm., and the acini measured 201 microns in diameter. The interlobular septums are still evident, and the acini are filled with colloid. *B*, a section from the thyroid gland of a patient aged 15 years. The gland weighed 13.5 Gm., and the acini measured 336 microns in diameter. The interlobular septums are indistinct, the colloid is dense and the acinar epithelium is low cuboidal. *C*, a section from the thyroid gland of a patient aged 22. The acini measured 475 microns in diameter. The thyroid gland reaches its largest size in early adult life.

except that there is more variability in their size within the individual gland (compare figs 6 *A* and 2 *C*). The range of variability in the size of the acini in the adult gland may extend from 50 to 400 microns. The acini of one individual gland remain fairly uniform; those from another may be on a larger or smaller scale (fig. 5 *A* and *B*).

Colloid goiter is represented by large acini filled with colloid. There is a great range of variability in the size of these acini within each gland (fig. 6 *C*). The acini average from 500 to 1,000 microns in diameter, and the weight of the gland is definitely greater. Localized areas of epithelial proliferation and acinar hyperplasia can be found. These have been called epithelial *Polster* by the German writers. All of the acini are not involved in this hyperplasia and are not to be confused with the acini in an exophthalmic goiter in which the hyperplastic changes are diffuse or, as they may be found, altered by the severity of the disease and the administration of iodine. In an exophthalmic goiter the acini are irregular in size and shape. They show infoldings of epithelial cells, and their lumen may be very irregular. They contain less colloid or poorly staining colloid. There may be areas in which the acini appear almost normal, but when medication (iodine) is not used the characteristic irregularity of the acini will be found in variable degree (fig. 7 *A*). If the acini appear normal in representative sections of the gland, it can be definitely stated that the patient did not suffer from exophthalmic goiter. The hypertrophy and hyperplasia of exophthalmic goiter are associated with a decrease in the colloid content of the acini and columnar epithelial cells of the acini to distinguish them from the epithelial *Polster* of colloid goiter, in which the colloid material stains normally.

THE ACINAR EPITHELIUM

The acinar epithelium can also be found to be somewhat variable at different stages in the development. In infancy it is cuboidal (fig. 2). As the acini increase in size, the epithelial cells lining them become flatter, so that during adult life the acinar epithelial cells are mostly flat or low cuboidal (fig. 4 *B* and *C*). As a person grows older the epithelial cells again become cuboidal concomitant with the decrease in the size of the acini. Columnar epithelial cells are rarely found in the acini of the normal thyroid gland, and if they do occur they are found only in small localized areas. The epithelial cells of a colloid goiter are much flattened (fig. 6 *C*). Those of an exophthalmic goiter are columnar, characteristic of the hypertrophy and hyperplasia of the disease (fig. 7 *A*).

THE INTERACINAR EPITHELIUM

In the normal thyroid gland the interacinar epithelial cells are found to decrease in number as the acini become larger. In puberty and early

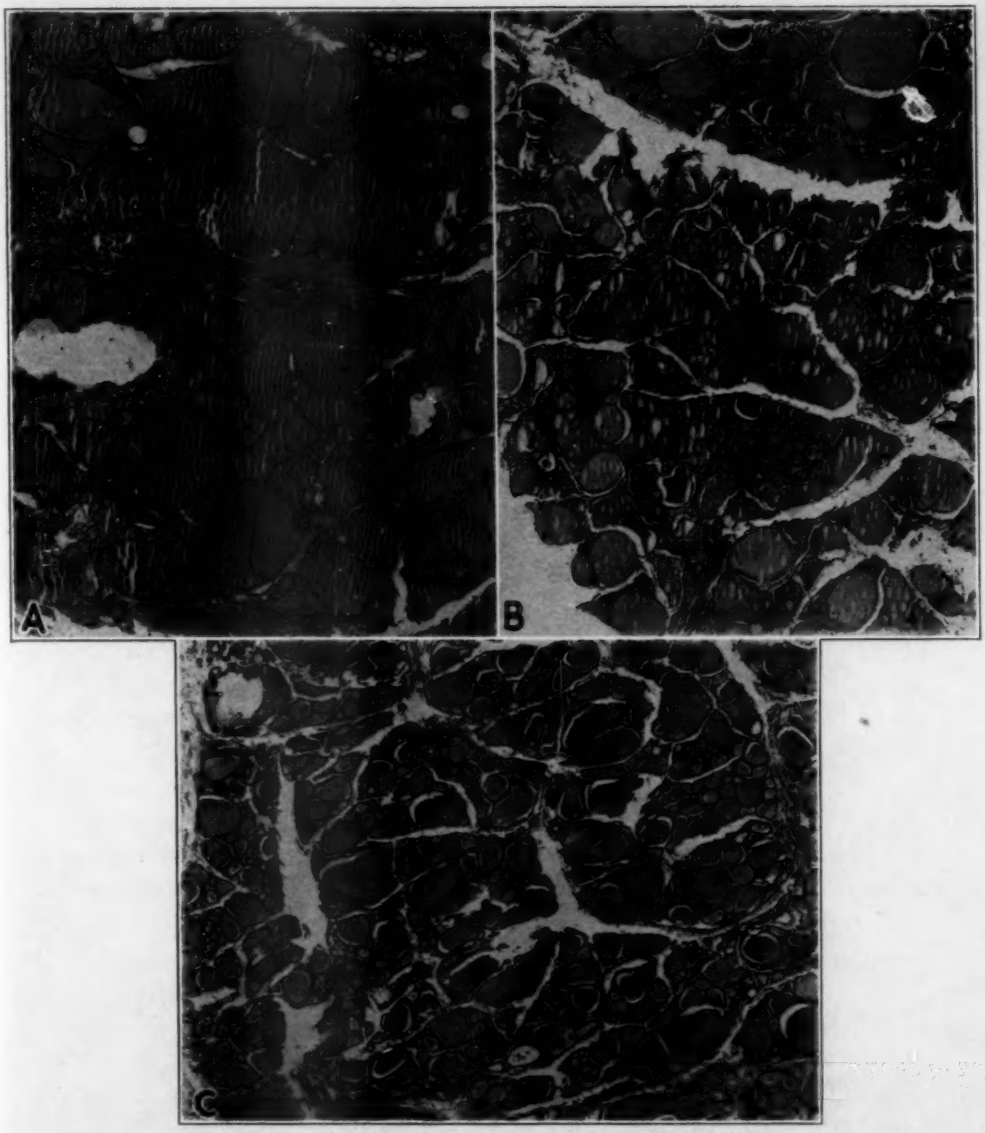

Fig. 5.—*A*, a section from the thyroid gland of an adult aged 39. The gland weighed 39 Gm., and the acini measured 336 microns in diameter. The acini are well filled with colloid and are beginning to show less uniformity in size than those from younger persons. As the person grows older, the lack of uniformity becomes more evident, as indicated in figures 5 *B* and *C* and 6 *A* and *B*. The acinar epithelium is cuboidal and flat. *B*, a section from the thyroid gland of an adult aged 45. The gland weighed 27.2 Gm., and the acini measured 252 microns in diameter. The interacinar epithelium is more abundant than in *A*. *C*, a section from the thyroid gland of an adult aged 55. The gland weighed 14.9 Gm., and the acini measured 168 microns in diameter. The interlobular septums are becoming more evident.

adult life the thyroid structure is composed almost completely of acini with no interacinar epithelial cells (figs. 4 *B* and *C*). In infancy and old age the interacinar epithelial cells are found more abundantly (figs. 2 *A* and *B* and 6 *A* and *B*).

The interacinar epithelial cells are not abundant in a colloid goiter. They appear between the acini at the sites of epithelial *Polster* (fig. 6 *C*).

The hyperplastic changes occurring in hyperthyroidism are also manifest by an increase in the interacinar epithelial cells, but these are associated with infoldings of the acini, columnar epithelial cells and decreased colloid content (fig. 7 A). So these changes should be easily distinguished from those which occur in the normal thyroid gland in infancy or in advanced age. In speaking of interacinar epithelial cells, I am not unaware of the fact that Reinhoff mentions that these cells are not situated in the interacinar spaces but are parts of other acini. I have merely chosen to designate them in that manner because of the illusion which they portray in a flat histologic section.

THE INTERLOBULAR STROMA

The interlobular stroma in the normal thyroid gland is found to be variable, depending on age. In infancy it is not uncommon to find large bands of interlobular stroma which appear to set off the acini into groups completely separated from one another (fig. 2 *A* and *B*). In puberty and early adult life these broad strands of interlobular stroma appear less distinct (figs. 4 *B* and *C* and 5 *A*).

It is often difficult to determine the boundaries of the lobule at this stage of development. As a person grows older, these broad strands of interlobular stroma again appear (fig. 6 *A*).

The presence of large bands of interlobular stroma in the thyroid gland of a person past middle life, therefore, should not lead one to conclude that some disease process has been the cause of this change. These structures are physiologically normal and may be found in the infantile and the senile thyroid. These bands of interlobular stroma should likewise not be interpreted as fibrous tissue proliferation such as occurs in the inflamed gland. This type of fibrous tissue proliferation invades the lobule and may, by its presence, destroy the acini. The bands of stroma within a nodule must not be interpreted as interlobular. These bands end blindly, whereas the interlobular stroma follows through so as to form the boundaries of an independent lobule (fig. 4 *A*). Because this stroma becomes less evident in the adult gland, it is often difficult to follow the bands out to their termination (fig. 5 *A* and *B*).

NODULES

There is still another change which occurs in a certain percentage of otherwise normal thyroid glands which often leads to confusion in the interpretation of diseases of the thyroid gland, that is, the presence of nodules.

A nodule is a localized area of new growth having its origin within a lobule. The consensus at this time is in accordance with the views of Hitzig and Michaud, who expressed the belief that these nodules had their origin as the result of development from normal thyroid tissue by metaplasia of the epithelial cells within a localized area, the normal thyroid tissue being displaced so as to form a complete secondary lobule or nodule.

Nodules may be classified histologically into four groups: colloid, parenchymatous (fetal), mixed and degenerate. The colloid nodule is one in which the acini are large and filled with colloid (fig. *7 C*). The parenchymatous nodule is one in which there are small acini, giving the appearance of the fetal thyroid, or solid packs of epithelial cells. The mixed nodule has been designated as one in which the histologic structure of both the parenchymatous and the colloid nodule is present. The degenerate nodule is one in which there are degenerative changes, such as hemorrhage, cystic formation, calcification and hyalinization. These changes may occur in any of the other types of nodules.

The histologic structure of these nodules may be extremely variable. There may be all sizes and shapes of acini; the epithelial cells may be small, and the interacinar epithelium may be abundant or sparse. Occasional bands of fibrous or hyaline stroma may be seen, but no true interlobular stroma can be identified within a nodule. No definite correlation can be made between the histologic structure within the nodule and the clinical symptoms of the patient.

The thyroid tissue adjacent to the nodule may be compressed and thereby altered (fig. *7 C*), but more remote sections have failed to disclose any pathologic changes which might have been attributed to the nodule. The presence of a nodule in a gland does not alter the histologic structure of the remaining portion of that gland, except as its presence may alter the adjacent tissue. Likewise, the presence of a toxic adenoma has failed to show evidence of having altered the remaining parenchyma of the thyroid.

Nodules are rarely if ever observed in the thyroid gland in infancy. They have their inception at puberty or later. At puberty 2 or 3 per cent of persons have nodules within their thyroid glands. This incidence increases rapidly with the advance in age. Roughly, this incidence in Minnesota may be represented by the same figure as the age of the

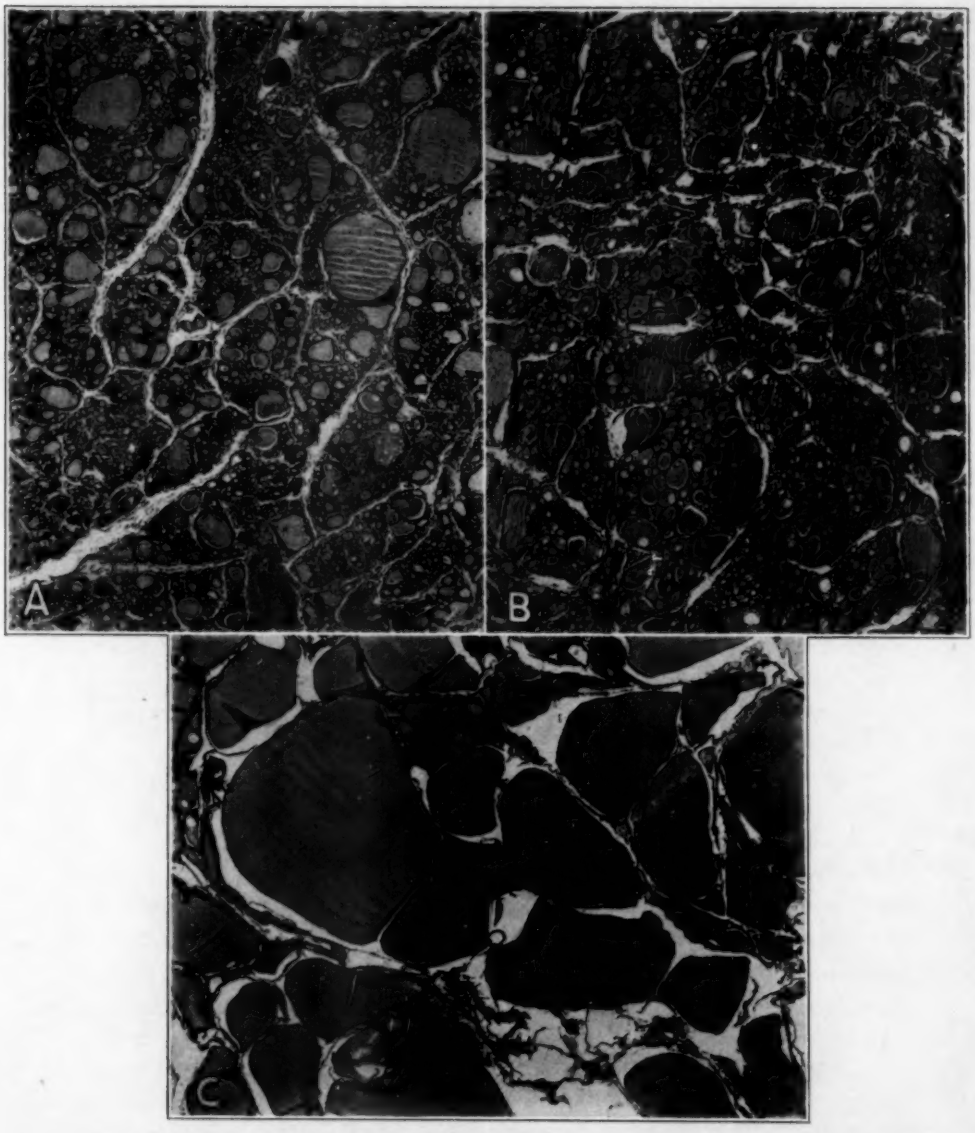

Fig. 6.—*A*, a section from the thyroid gland of a person aged 67. The gland weighed 30 Gm., and the acini measured 117 microns in diameter. Most of the acini are small. A few are large. The interlobular septums are distinct, and the interacinar epithelium is more abundant than in preceding sections. *B*, a section from the thyroid gland of an 86 year old patient. The gland weighed 21.3 Gm., and the acini measured 117 microns in diameter. The structure is approaching that of the infantile thyroid in many respects. *C*, a section from the thyroid gland of a boy aged 16 years. The goiter had been present for eight years, and the basal metabolic rate was minus 7. No iodine therapy was given preoperatively. The gland was diffusely enlarged. A diagnosis of colloid goiter was made. Note the epithelial *Polster* and large acini.

group of persons under consideration; for example, approximately 30 per cent of persons at 30 years of age have nodules within their glands (fig. 8). In old age most of the glands can be found to contain nodules within their structure.

It is not intended to infer that all these nodules are clinically palpable but that they are found macroscopically when gross serial sections are made through glands which have been removed at autopsy from patients dying from other causes than from diseases of the thyroid gland.

The development of these nodules has been attributed by some authors to the physiologic strains encountered during a life time. In favor of this opinion, puberty and the child-bearing period have been cited as examples of physiologic stress. In corroborating these assumptions with the demonstrable facts, it is found that the incidence of nodules at puberty in both males and females makes an abrupt rise over that of the prepuberty period. A similar increase in the incidence is not observed in the male at the period corresponding to the child-bearing period for the female (fig. 8).

At 34 years of age, the average age of patients with exophthalmic goiter, approximately 34 per cent of the normal glands contain nodules. Therefore, it should not be unreasonable to suppose that 34 per cent of the glands from patients suffering from exophthalmic goiter will contain nodules within their structure. This fact was clearly demonstrated in a previous paper.[13] The presence of a nodule, therefore, should not confuse the clinician to the extent of stimulating him to call every exophthalmic goiter in which a nodule can be demonstrated a toxic adenoma. This has been investigated in another way on the assumption that exophthalmos is a sign found only in the patient whose gland shows diffuse hypertrophy and hyperplasia.

Among 121 goiters at the Minnesota General Hospital which were diagnosed clinically as toxic adenoma, there were 10 from patients who showed exophthalmos on physical examination. The study of these 10 patients who presented clinical signs and symptoms characteristic of exophthalmic goiter, including exophthalmos, convinced me that the growth was wrongly diagnosed as toxic adenoma because of the presence of palpable nodules. A diagnosis of exophthalmic goiter should have been made on the basis of the exophthalmos. All these glands were reexamined. In each the parenchymatous portion of the gland, i. e., that portion of the gland outside the nodule, showed hypertrophy and hyperplasia in a more or less marked degree (fig. 7 *A* and *B*). This finding was significantly absent in those cases of toxic adenoma in which the

13. Rice, Carl O.: Incidence of Nodules in the Thyroid, Arch. Surg. **24**:505-515 (March) 1932; Exophthalmic Goiter Versus Toxic Adenoma, Minnesota Med. **17**:361-364, 1934.

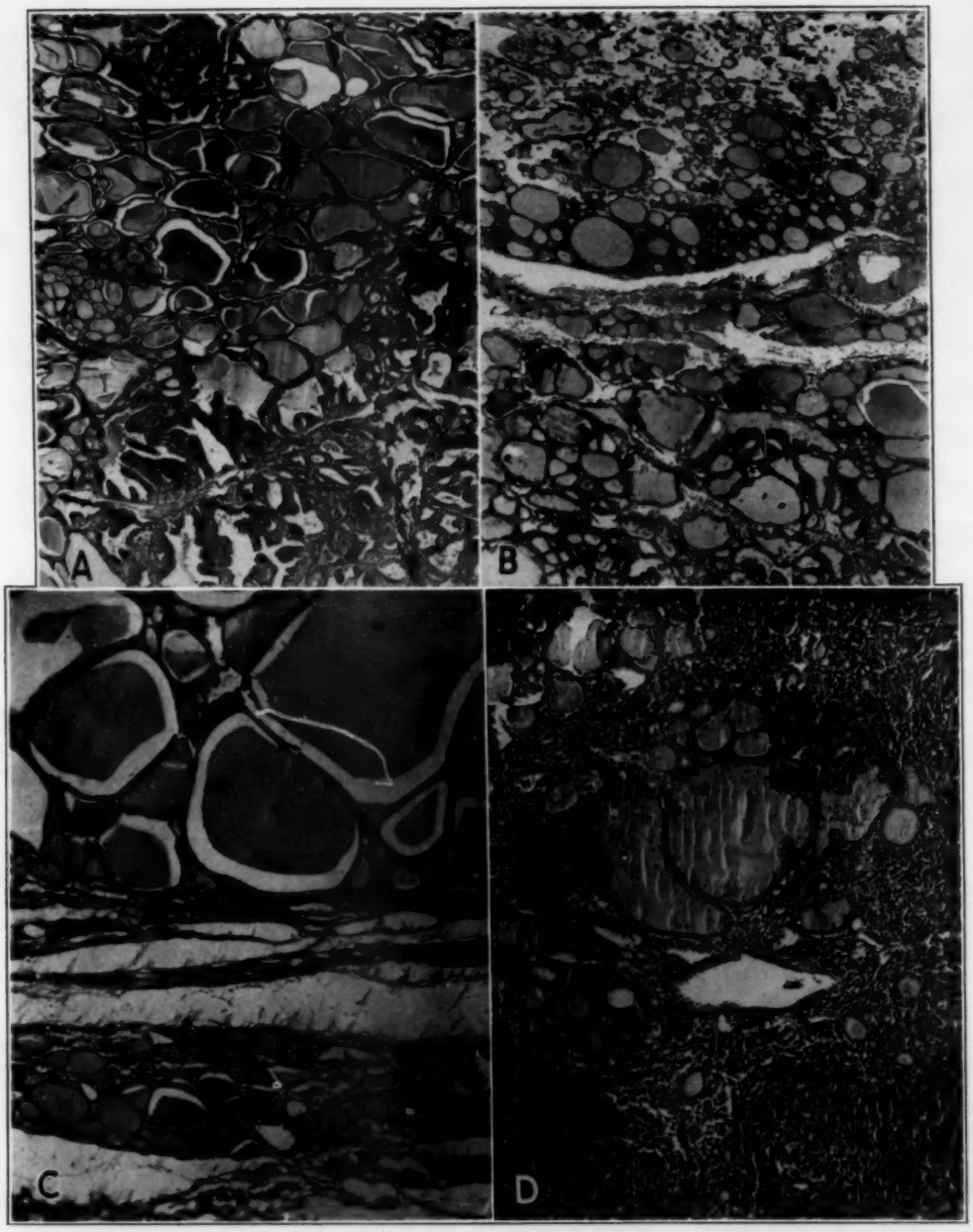

Fig. 7.—*A*, a section from the thyroid gland of a woman aged 24, who presented typical symptoms of hyperthyroidism. There was no exophthalmos, and the basal metabolic rate was plus 80 per cent. No nodules were found within the gland. The diagnosis was exophthalmic goiter. *B*, a section from a goiter of a man aged 42, who had typical signs and symptoms of exophthalmic goiter, including exophthalmos and a basal metabolic rate of 20 plus. There is one nodule in the gland 4 cm. in diameter. The nodule shows the typical structure of a fetal adenoma. The adjacent tissue shows hypertrophy and hyperplasia similar to that in *A*. *C*, a section from a fetal adenoma, showing a colloid nodule at the top, a compressed capsule in the center and normal thyroid tissue at the bottom. *D*, a section of an exophthalmic goiter, showing diffuse parenchymatous hypertrophy and hyperplasia (center) with marked lymphoid hyperplasia and germinal centers (bottom). These should not be mistaken for exudative thyroiditis.

patients did not have exophthalmos. In these, the histologic structure of the parenchymatous portion of the gland contained normal acini (fig. 7 *C*).

Most writers will agree that the histologic changes in an exophthalmic goiter consist of diffuse parenchymatous hypertrophy and hyperplasia, which are altered only by the severity of the disease and the administration of iodine. The histologic changes in a toxic adenoma have not been as uniformly decided. Some writers have observed hypertrophy and hyperplasia within the nodule with no changes of the parenchymatous portion of the gland, whereas others have observed hypertrophy and hyperplasia both inside and outside the nodules, and thereby have been led to believe that toxic adenoma and exophthalmic goiter present essentially the same pathologic changes. I am of the opinion that the latter picture is that of exophthalmic goiter.

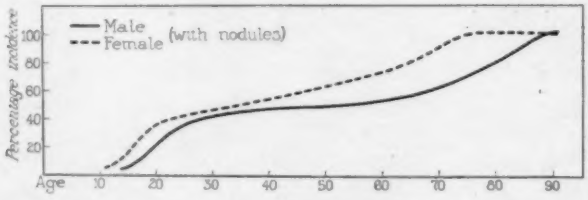

Fig. 8.—Curves showing the incidence of nodules in the thyroid gland during a life span.

Lymphocytic foci may be found in 10 per cent of the normal glands, but they are never as extensive as may be observed in an exophthalmic goiter or in an inflamed gland. Lymphoid hyperplasia is not uncommon in exophthalmic goiter and may frequently be extensive. This finding in the presence of epithelial hypertrophy and hyperplasia should be recognized as part of the picture of exophthalmic goiter and should not be confused with the exudative phase of thyroiditis (fig. 7 *D*). Epithelial desquamation is not found in the normal thyroid gland, whereas it is one of the characteristic features in an exophthalmic goiter.

CONCLUSIONS

The histologic structure of the normal thyroid gland may vary extensively. These variations are somewhat dependent on age and also on locality.

As a person passes through life the thyroid gland increases in weight, reaching its maximum during early adult life, after which it again gradually decreases to the end of the life span.

The acini increase or decrease in size as the weight of the gland changes. The acinar epithelium may vary from flat to cuboidal. No columnar cells are found in the normal gland.

The presence of a nodule within a thyroid gland does not produce pathologic changes in the remote portions of that organ.

Diffuse parenchymatous hypertrophy and hyperplasia can occur in a gland containing nodules but will be manifest clinically by typical signs and symptoms of exophthalmic goiter as distinguished from those of toxic adenoma.

Nodules may be found in an otherwise normal thyroid gland. Their incidence increases with an increase in age. They probably represent a physiologic response to stimuli during life. Their presence in a toxic goiter does not necessarily indicate that they are the source of the hyperthyroidism.

The variations in the structure of the normal thyroid gland must be taken into consideration in order to interpret properly the changes in the diseased gland.

SUBPHRENIC ABSCESS

A REVIEW OF ONE HUNDRED AND ELEVEN CASES AND A RÉSUMÉ OF THE SUBJECT

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This article is presented with the purpose of giving a review of 111 cases of subphrenic abscess, together with a résumé of the subject. The material was collected from 21,430 case records of patients admitted to the Jewish Hospital from 1916 to 1935 inclusive. The experience at this hospital with the extraperitoneal approach to a subphrenic abscess, with 6 deaths in 71 cases, or a mortality of 8.5 per cent, has encouraged me to present this communication, as these figures are considerably lower than those generally reported. In the twenty years that this procedure has been intermittently employed, a method of approach has been evolved which in many respects is similar to the one recently suggested by Ochsner and Graves.[1] There are, however, some technical differences in the procedure, detailed toward the end of this paper, which may help to simplify the approach.

The relatively good operative results obtained in the uncomplicated cases in the first decade of this study may be ascribed to the fact that the diagnosis was uncertain. During this period it was found that in the early stages of the abscess no sharp line of differentiation could be drawn between a subphrenic abscess and a perinephric abscess; but, because of their anatomic proximity, it was felt that a lumbar retroperitoneal approach could be used with advantage in either case. When the results of this method of drainage in the verified cases of subphrenic abscess were reviewed, it was found that the mortality was considerably less than that reported in the literature, and therefore in the subsequent cases of subphrenic abscess the approach was made through the lumbar extraperitoneal route. In the first decade this approach was used in 29 cases of subphrenic abscess, with 3 deaths, or a mortality of 10.4 per cent. Later (in the second decade), as the diagnosis was made earlier and attempts were made to drain the abscess promptly, other routes were tried, with comparatively poor results, necessitating a return to the extraperitoneal route. In the second decade the transserous route was used in 19 cases, with 10 deaths, or a mortality of 52.5 per cent. In this same period the extraperitoneal route was employed in

From the Department of Surgery, the Jewish Hospital.

1. Ochsner, A., and Graves, A. M.: Subphrenic Abscess, Ann. Surg. **98**:961, 1933.

42 cases, with 3 deaths, or a mortality of 7.1 per cent. These statistics present further evidence of the better results obtainable in the extraperitoneal drainage of a subphrenic abscess.

In this study I have further investigated the various surgical procedures employed for specific intra-abdominal conditions and their relationship to the incidence of subphrenic abscess. The results of this study are given in detail in table 1.

TABLE 1.—*Statistical Résumé and the Incidence of Subphrenic Abscesses in Cases of Intra-Abdominal Conditions in Which Operation Was Performed*

Pathologic Conditions and Operations	Number of Cases 1916-1935	Number and Percentage of Subphrenic Abscesses
Diseases of the appendix	13,535	26 (0.20)
Appendectomy without drainage	10,437	5 (0.05)
Appendectomy with drainage	3,017	8 (0.23)
Drainage without appendectomy	81	13 (16.05)
Diseases of the biliary passage	2,679	35 (1.3)
Cholecystectomy	734	5 (0.7)
Cholecystectomy with prophylactic appendectomy	1,319	4 (0.3)
Cholecystostomy or cholecystenterostomy	501	18 (3.6)
Choledochotomy or choledocostomy	126	3 (2.4)
Diseases of the liver	59	3 (5.1)
Incision and drainage of abscess of the liver	59	3 (5.1)
Diseases of the stomach and esophagus	694	5 (0.7)
Suture of perforated gastric ulcer	64	4 (6.2)
Gastro-enterostomy for gastric ulcer	166	0
Gastrostomy for gastric and esophageal growth	121	1 (0.8)
Gastrectomy for carcinoma of stomach	224	0
Gastro-enterostomy for a malignant growth	119	0
Diseases of the pylorus and duodenum	551	1 (0.18)
Ramstedt's pyloroplasty	114	0
Gastro-enterostomy for duodenal ulcer	285	0
Suture of perforated duodenal ulcer	152	1 (0.66)
Diseases of the intestines	596	1 (0.17)
Enterostomy with relief of obstructing adhesions	212	0
Entero-enterostomy for neoplasm	234	0
Suture of ruptured intestine	32	1 (3.1)
Reduction of intussuception	55	0
Cecostomy	63	0
Diseases of the rectosigmoid	674	0
Resection for carcinoma of the rectosigmoid	674	0
Diseases of the pelvis	478	8 (1.7)
Salpingitis	344	2 (0.9)
Pelvic abscess	134	6 (4.5)
Perinephritic abscess—incision and drainage	19	5 (26.3)
Exploratory laparotomy without drainage	718	0
Exploratory laparotomy with drainage of intraperitoneal abscess of unknown etiology	83	4 (4.7)
Incision and drainage of an abscess of the abdominal wall	44	1 (2.3)

HISTORICAL REVIEW

The early literature on subphrenic abscess, which presents an isolated case found at autopsy,[2] a controversial diagnostic problem, the solution of which was obtained at necropsy,[3] and sporadic papers calling the

2. Louis, P.: Mémoires, ou recherches anatomico-pathologiques sur le ramollissement avec amincessement et sur la destruction de la membrane muqueuse de l'estomac, Paris, Gabon & Cie, 1826, p. 367.

3. Barlow, G. H.: Perforation of the Stomach with Obscure Thoracic Symptoms, London M. Gaz. **1**:13, 1845.

attention of the medical profession to the condition,[4] culminates with Maydl's monograph [5] on the subject, published in 1894. Thereafter the subject attracted little attention until four years later, when Martinet [6] presented the results of a systematic investigation into the anatomic varieties of subphrenic abscess. This comprehensive contribution marked a distinct epoch in the study of infections in the subphrenic area and later gave impetus to Box and Eccles' [7] and Barnard's [8] anatomic subdivisions of this area. Based on these later works, Piquand,[9] Eisendrath [10] and Ochsner and his co-workers [11] evolved the modern conception of the management of subphrenic infections. Until recently most cases of subphrenic abscess went unrecognized, and the patient either recovered spontaneously or more frequently succumbed to the malady. With the increase in knowledge acquired from extensive abdominal and thoracic operations and with more accurate diagnostic aids, there are more cases in which the condition is recognized and treated at an early stage. It is still unfortunately true, however, that infections in the subphrenic area occur more frequently than is commonly supposed.

The terms which have been used in the literature more or less synonymously with subphrenic abscess are: perigastric abscess (Barlow), suprahepatic abscess (Bernheim), false pneumothorax (Cossy), pneumoperforative peritonitis (Sanger), hepatoperitoneal abscess (Ferol), pyopneumothorax subphrenicus (Leyden), subphrenic empyema, hypophrenic abscess, subphrenic peritonitis, subdiaphragmatic abscess and others.

ANATOMY

The subphrenic area is limited above by the diaphragm and below by the transverse colon and its mesentery. This area is composed of two main subdivisions: an intraperitoneal area and an extraperitoneal

4. Leyden, E.: Ueber Pyopneumothorax subphrenicus, Ztschr. f. klin. Med. **1**:320, 1879. Pfuhl: Ein oberhalb der Leber gelegenes peritonitisches Exsudat in die rechte Lunge perforirt, mit den Zeichen eines rechtsseitigen Pyopneumothorax, Berl. klin. Wchnschr. **5**:57, 1877. Volkman, R., cited by Bogart.[24]

5. Maydl, K.: Ueber subphrenische Abscesse, Vienna, Joseph Safar, 1894.

6. Martinet, A.: Des variétés anatomiques, d'abcès sous-phrénique, Thèse de Paris, no. 84, 1898.

7. Box, C. R., and Eccles, W. M.: Clinical Applied Anatomy, Philadelphia, P. Blakiston's Son & Co., 1906.

8. Barnard, H. L.: Surgical Aspects of Subphrenic Abscess, Brit. M. J. **1**: 371 and 429, 1908.

9. Piquand, G.: Les abcès sous-phréniques, Rev. de chir. **39**:156, 1909.

10. Eisendrath, D. N.: Complications of Appendicitis, S. Clin., Chicago **1**: 1035, 1917.

11. (*a*) Ochsner, A.: Subphrenic Abscess: Its Diagnosis and Treatment, with Special Reference to the Extraperitoneal Operation, Internat. Clin. **2**:79, 1931. (*b*) Ochsner, A.; Gage, I. M., and Garside, E.: The Intra-Abdominal Post-Operative Complications of Appendicitis, Ann. Surg. **91**:544, 1930.

area. The liver divides the intraperitoneal area into a suprahepatic area and an infrahepatic area, each of which is composed of three smaller limited areas (figs. 1 and 2).

The Suprahepatic Intraperitoneal Area.—This area is composed of: (1) the left suprahepatic area, located above the liver and to the left of the left lateral ligament, which in turn is a prolongation to the left of the coronary ligament; (2) the right anterior suprahepatic area, located above the liver, to the right of the coronary ligament and in front of the right lateral ligament, and (3) the right posterior suprahepatic area, located above the liver and behind the right lateral ligament.

The Infrahepatic Intraperitoneal Area.—This area is composed of: (1) the right infrahepatic area, located below the liver and to the right

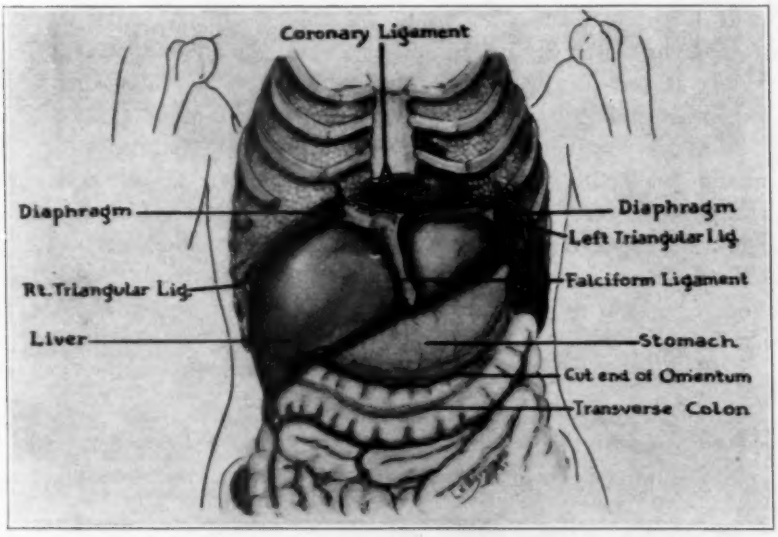

Fig. 1.—An anterior view of the upper portion of the abdomen with exposure of the subphrenic area. The diaphragm is shown elevated to expose the suprahepatic area, and the great omentum is cut away from the stomach to expose the transverse colon. The subphrenic area is bounded above by the diaphragm and below by the transverse colon and its mesentery.

of the round ligament of the liver and the ligament of the ductus venosus; (2) the left anterior infrahepatic area, located below the liver and to the left of the round ligament and the ligament of the ductus venosus and in front of the stomach, and (3) the left posterior infrahepatic area, located below the liver and to the left of the round ligament and the ligament of the ductus venosus and behind the gastrohepatic omentum.

The Extraperitoneal Area.—This area is composed of: (1) the anterior extraperitoneal area, located between the anterior external surface of the parietal peritoneum and the internal surface of the upper anterior

abdominal wall below the diaphragm (this area may be arbitrarily divided into a right and a left side by a midabdominal line); (2) the right posterior extraperitoneal area, located between the posterior external surface of the parietal peritoneum and the upper posterior abdominal wall below the diaphragm and to the right of the inferior leaf of the coronary ligament (this area includes the bare area of the liver), and (3) the left posterior extraperitoneal area, located between the posterior external surface of the parietal peritoneum and the upper posterior abdominal wall below the diaphragm and to the left of the inferior leaf of the coronary ligament.

Subdivisions.—The literature deals adequately with the anatomic subdivisions of the intraperitoneal area. However, subdivisions of the extraperitoneal area have received almost no consideration. It is the

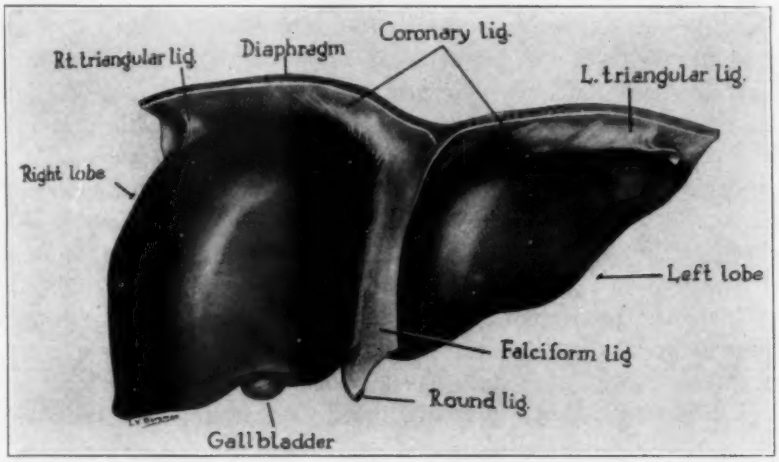

Fig. 2.—The liver, showing its ligamentous attachments which subdivide the suprahepatic subphrenic area. The diaphragm and its peritoneal attachments and reflections above the liver are shown in detail.

further purpose of this paper to call the reader's attention to these subdivisions and to point out the sources, the location and the incidence of infections of the extraperitoneal areas (see table 3). Many investigators refer to an "extraperitoneal" area, having in mind only the region of the bare area of the liver.

ETIOLOGY

Subphrenic abscess usually follows a suppurative process elsewhere in the body and generally one in the abdomen. It is rarely primary. Schwartz [12] reported 8 cases of so-called primary subphrenic abscess,

12. Schwartz, J.: Suppuration in the Subphrenic Region, with Special Reference to Primary Idiopathic Liver and Subphrenic Abscess, Arch. Surg. **20**:317 (Feb.) 1930.

which most investigators believe to have been hematogenous infections secondary to the grip.

The subphrenic area may become infected: (1) by direct extension from the peritoneum and contiguous organs—the liver, gallbladder, duodenum, stomach, kidney, spleen, pancreas, etc.; (2) by distant extension from an appendical abscess, a pelvic infection, an infection of the skin on the lower part of the thorax or the upper part of the abdomen, the umbilicus, etc.; (3) by rupture into the subphrenic area from an abscess of the liver, a hydatid cyst of the liver, osteomyelitis of a rib or vertebra, empyema thoracis, etc.; (4) by a retrograde lymphatic infection from an empyema thoracis, pneumonia, abscess of the lung, etc.; (5) by metastatic infection from elsewhere in the body, as furunculosis, osteomyelitis, septicemia, influenza, etc., and (6) by direct implantation or injury to an anatomically related organ following a penetrating trauma.

1. *Direct Extension from the Peritoneum and Contiguous Organs.*—The most important and frequent extensions are those which follow or accompany peritonitis. A patient in the recumbent position or slightly tilted toward the Trendelenburg or Fowler position will create two independent intraperitoneal areas, one in the cul-de-sac of Douglas and the other in the posterior part of the subdiaphragmatic area. These two areas are separated from each other by the normal curvature of the lumbar portion of the spine. As a result, stagnation rather than dependent drainage will take place. If the patient is further tilted into the Trendelenburg position, dependent drainage will take place into the subphrenic area rather than away from it. Additional factors which will help spread infection up into the subphrenic area are the constantly changing intra-abdominal pressure during respiration and the suction effect of the diaphragm.

In order that a renal infection may give rise to a subphrenic abscess, the infection must first extend outside the kidney proper as a perinephric abscess. It then extends upward across the kidney, over the liver and through the foramen of Winslow into the lesser peritoneal cavity, or it may dissect its way up on the outside of the peritoneum and reach the area over the liver, lying between the external parietal peritoneum and the diaphragm.

An extramural spill from any organ intimately related to the subphrenic area will cause a localized abscess in the vicinity of the perforation, in the lesser sac or in the subdiaphragmatic area.

In the present series of cases of known etiology (table 2), 59 (62.8 per cent) were due to direct extension from the peritoneum and contiguous organs.

2. *Distant Extension.*—The appendix may be taken as an example of an infection from a distant focus producing subphrenic abscess.

Infections of the subphrenic area following appendicitis may take place: (*a*) as a result of a generalized peritonitis secondary to a ruptured appendix, (*b*) as a result of an abscess of the liver following an infected thrombophlebitis arising from the appendix, (*c*) through infection of the posterior cellular spaces, (*d*) through the lymphatics, and (*e*) as a result of an ascending infection extending along the paracolic gutter.

(*a*) The first type has been considered under section 1.

(*b*) The second type will be considered under section 3.

(*c*) Aschoff [13] has shown that there are four layers of lymphatics in the wall of the appendix, all of which drain into the meso-appendix. Munro [14] pointed out that infections in the lymphatics of the meso-

TABLE 2.—*Etiology of 111 Subphrenic Abscesses*

Organ	Number of Cases	Total Percentage
Stomach and duodenum	6	5.4
Gastric ulcer with perforation	4	3.6
Perforated carcinoma of the stomach	1	0.9
Perforated duodenal ulcer	1	0.9
Appendix	26	23.4
With generalized peritonitis	13	11.7
Liver and biliary passages	38	34.2
Abscess of liver	3	2.7
Diseases of the biliary passage with localized peritonitis at the time of operation on the biliary passage	13	11.7
Kidney	5	4.5
Female genitalia	2	1.8
Pelvic abscess	6	5.4
Prostatic abscess	1	0.9
Intestine	1	0.9
Empyema	1	0.9
Pneumonia	3	2.7
Abscess of the lung	1	0.9
Typhoid of the spine	1	0.9
Furunculosis	1	0.9
Grip	2	1.8
Unknown causes	17	15.3

appendix may be carried back to the retroperitoneal cellular space above and behind the cecum. From here the infection spreads up into the retroperitoneal cellular spaces behind the ascending colon and in front of the kidney to the subdiaphragmatic space. If, in addition, the appendix is under the liver or is retrocecal or associated with an abscess, the possibilities of the formation of a subphrenic abscess are greatly enhanced. Frequently, in the removal of an inflamed appendix which is adherent to the posterior parietal peritoneum, the appendix is torn away from its attachments, leaving a piece of infected necrotic tissue behind, or a part of the surface of the peritoneum is pulled away with the appendix. In either case a raw and infected surface is left through

13. Aschoff, L.: Appendicitis: Its Aetiology and Pathology, translated by G. C. Pether, London, Constable & Co., Ltd., 1932.

14. Munro, J. C.: Lymphatic and Hepatic Infections Secondary to Appendicitis, Ann. Surg. **42**:692, 1905.

which organisms may reach the retroperitoneal cellular spaces and lymphatics and from there be carried to the subphrenic space.

(*d*) McCallum [15] in 1903 and Clarke [16] about the same time independently found that the lymphatics of the general abdominal cavity tend to concentrate below the diaphragm. Lemon and Higgins [17] have shown that substances injected into the peritoneal cavity will frequently appear in the thorax via the lymphatics. Cunningham [18] later pointed out that before this material appears in the thorax there will be an accumulation of the injected material below the diaphragm. It is this lymphatic stream which similarly carries infected material to the subphrenic area. Specifically, as regards appendicitis, I quote Truesdale: [19]

> . . . we have studied the lymphatics in their course from the appendix to their distribution in the region about the diaphragm. The bacillus-laden lymph passes from the appendiceal abscess to the appendicular nodes which communicate with the ileocecal nodes. The stream then empties into the lymphatic trunk following the superior mesenteric vein which in turn empties into the portal vein.

From here, according to Truesdale, the lymphatics extend along the surface and through the liver, to the dense network of lymphatics along the line of attachment of the falciform ligament. The lymphatics then pass to the upper area of the liver where the infection may localize and there form a subphrenic or subdiaphragmatic abscess.

(*e*) The paracolic gutter along the ascending colon forms a natural fold or channel along which infections in the vicinity of the cecum may extend upward to the inferior surface of the liver. The infection may then pass upward along the lateral surface of the liver to involve both the right infrahepatic and the suprahepatic space. In the present series of cases of known etiology, 22 (23.4 per cent) were due to extensions from a distant focus.

3. *Rupture into the Subphrenic Area.*—In cases of rupture into the subphrenic area, a preexisting localized infection near the subphrenic area ruptures into it. This process can be readily understood in the case of an abscess of the liver giving rise to a subphrenic abscess. However, in the case of an empyema thoracis, the process may take place either (1) by perforation of the pleura and diaphragm, thereby allowing

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15. McCallum, W. G.: On the Mechanism of Absorption of Granular Material from the Peritoneum, Bull. Johns Hopkins Hosp. **14**:105, 1903.

16. Clarke, cited by Munro.[14]

17. Lemon, W. S., and Higgins, G. M.: Lymphatic Absorption of Particulate Matter Through the Normal and Paralysed Diaphragm, Tr. A. Am. Physicians **44**:148, 1929.

18. Cunningham, R. S.: The Physiology of Serous Membranes, Physiol. Rev. **6**:242, 1926.

19. Truesdale, P. E.: The Origin and Course of Infection in Subphrenic Abscess, Ann. Surg. **98**:846, 1933.

the pleural contents to enter the subdiaphragmatic space, or (2) by an infection producing a lymphatic block in the chest, which extends back to the subphrenic area. (This phase will be considered in detail under the heading "4. Retrograde Lymphatic Infection from the Thorax.") In the present series of cases of known etiology, 5 (5.3 per cent) were due to rupture into the subphrenic area.

4. *Retrograde Lymphatic Infection from the Thorax.*—Schlanger [20] injected a radiopaque material into the subphrenic area and studied its spread through the lymphatics by means of roentgenograms. He was able to show retropleural lymphatic extensions into the hilar area of the lung. In the case of a subphrenic abscess secondary to empyema thoracis, pneumonia, abscess of the lung, etc., the thoracic lymphatics which communicate with the subphrenic area become infected. As a result of the lymphatic blockage which is set up, retrograde stagnation and infection take place. This process extends as far back as the dilated lymphatics on the inferior surface of the diaphragm. The lymphatics become increasingly distended with the infected material until they rupture, thereby producing an infection of the subphrenic area. In the present series of cases of known etiology, 5 (5.3 per cent) were due to retrograde lymphatic infections.

5. *Metastatic Infection.*—The existence of an infection which finds its way into the blood stream is presupposed. The infection is then carried to and deposited in the subphrenic area via the circulation. Such cases occur following furunculosis, osteomyelitis, septicemia, grip, etc., and are reported in the literature from time to time. In the present series of cases of known etiology, 3 (3.2 per cent) were due to metastasis.

6. *Direct Implantation.*—In cases of direct implantation, the subphrenic area is injured, as in a stab wound or gunshot wound of the lower part of the thorax or the upper part of the abdomen. Infection is carried into the subphrenic area with the traumatizing instrument, or the injury may have been sustained by an organ anatomically related to the subphrenic area, which, as a result of the injury, becomes a locus minoris resistentiae and subsequently ruptures into the subphrenic area. Injuries to the base of the lung, diaphragm, stomach and liver are included in this group. Although subphrenic abscess due to trauma is rare, it has been reported. In the present series of cases of known etiology, there were none due to trauma.

Summary.—Of Ochsner and Graves' [1] series of cases of subphrenic abscess, including those collected from the literature, 29.1 per cent arose from an infection in the stomach and duodenum, 30.6 per cent

20. Schlanger, P.: Las vías linfáticus del espacio subfrénico derecho, Rev. méd. latino-am. **13**:2244, 1928.

from an infection of the appendix and 12.1 per cent from an infection in the liver and biliary passages. In the present series of cases 5.4 per cent were due to an infection in the stomach and duodenum, 23.4 per cent to an infection in the appendix and 34.2 per cent to an infection in the liver and biliary passages (table 2). It is generally agreed that these three sources constitute between 65 and 75 per cent of all the sources of subphrenic abscesses. In table 3 I have tabulated the sources

TABLE 3.—*Source of Infection of the Various Divisions of the Subphrenic Space and the Incidence of These Infections in 90 of the Author's Cases*

Location	Etiology	Number of Cases	Percentage
Right posterior suprahepatic intraperitoneal space	Right diaphragm and pleura; pyloroduodenal region; paracolic gutter, draining appendix, cecum, pelvis, etc.; right infrahepatic area	18	20.0
Right anterior suprahepatic intraperitoneal space	Pyloroduodenal region; gallbladder	12	13.3
Right infrahepatic intraperitoneal space	Liver, gallbladder and biliary ducts; hepatic flexure of colon; pyloroduodenal region; right posterior suprahepatic area	32	35.5
Left suprahepatic space	Gastro-esophageal region	1	1.1
Left anterior infrahepatic space	Perforation of the anterior wall of stomach; liver and spleen	3	3.3
Left posterior infrahepatic space	Perforation of the posterior wall of stomach; pancreatitis and infected pancreatic cysts; spleen; leakage from a retrocolic gastro-enterostomy anastomosis; perforation of a gastrojejunal ulcer	4	4.4
Right posterior extraperitoneal space	Infection of bare area of liver; retrocecal appendix; right perinephric abscess; pancreatitis; suppuration of right lumbar and iliac glands; right side of thorax and diaphragm	8	8.9
Left posterior extraperitoneal space	Left perinephric abscess; diverticulitis of descending colon; suppuration of left lumbar and iliac glands; descending colon; pancreas; left side of thorax and of diaphragm	3	3.3
Left anterior extraperitoneal space	Lymphatics of the round ligament of the liver; lymphatics of the sheath of the rectus muscle; infections of abdominal wall	1	1.1
More than one space infected		4*	4.4
Infected space not determined		4	4.4

* These cases were not included in the table. In all 4 cases the infection involved both the right infrahepatic and the right posterior suprahepatic intraperitoneal space.

in the cases at the Jewish Hospital, the various areas which a subphrenic abscess may involve and the incidence of the infection in the various areas.

BACTERIOLOGY

The organisms found in subphrenic abscesses were investigated in 70 cases in the present series (table 4). Colon bacilli were present in 22 cases (31.7 per cent), streptococci in 21 (30.2 per cent) and staphylococci in 22 (31.7 per cent). Colon bacilli were found alone most frequently—in 16 (23 per cent) of the cases—and staphylococci were

found most frequently associated with other organisms—in 10 (14.4 per cent) of the cases. Barnard [8] and Whipple [21] reported the bacteriologic findings in a total of 44 cases in which series they found colon bacilli in 36 per cent of the cases, streptococci in 22.5 per cent and staphylococci in 15.8 per cent.

Cokkins [22] stated:

> It is surprising to find that Ochsner and Graves report this space [the right infrahepatic intraperitoneal] to have a less number of collections than the posterior, superior space. The explanation possibly is that most of the infections in this space subside more often than in the other spaces.

In Ochsner and Graves' series of cases collected from the literature the right posterior suprahepatic area was involved in 28.86 per cent and

TABLE 4.—*Organisms in 70 Cases of Subphrenic Abscess*

Organism	Number of Cases	Total Percentage
Bacillus coli	22	31.4
Streptococcus	21	30.2
Nonhemolytic streptococcus	11	15.7
Streptococcus haemolyticus	9	12.9
Streptococcus viridans	1	1.4
Staphylococcus	22	31.4
Staphylococcus aureus	13	18.6
Staphylococcus albus	9	12.8
Pneumococcus	4	5.7
Bacillus mucosus-capsulatus	2	2.8
Micrococcus catarrhalis	1	1.4
Bacillus subtilis	1	1.4
Gram-positive diplococcus and coccus	6	8.6
Gram-positive bacillus	1	1.4
Gram-negative bacillus	2	2.8
Organisms undetermined	10	14.3
More than one organism present	22	31.5

the right infrahepatic area in 8.9 per cent. In their own 50 cases, the right posterior suprahepatic area was involved in 60 per cent and the right infrahepatic area in 13.5 per cent. In the present series of 90 cases in which operation was performed the right posterior suprahepatic area was involved in 20 per cent and the right infrahepatic area in 35.5 per cent. While my statistics corroborate the view held by Cokkins, but those of Ochsner and Graves do not, I am of the opinion that the explanation offered by the former is not entirely warranted. According to Ochsner and Graves' statistical résumé and the opinion of many other investigators, the stomach and duodenum, the appendix and the liver and biliary passages constitute the three greatest sources of sub-

21. Whipple, A. O.: A Study of Subdiaphragmatic Abscess, Am. J. Surg. **40**: 1, 1926.

22. Cokkins, A. J., in Maingot, R.: Post Graduate Surgery, New York, D. Appleton-Century Company, Inc., 1936, vol. 1.

phrenic abscesses. Therefore a discussion of these three sources may help explain the aforementioned difference of opinion.

It is not unlikely that in a goodly proportion of the cases of subphrenic abscess of gastric origin collected by Ochsner and Graves the original lesion was in the region near the pylorus. In such cases, as well as in those of duodenal origin, a greater number of the abscesses occur in the right infrahepatic area than in the right posterior suprahepatic area. It is generally agreed that an appendical pathologic process is more often followed by involvement of the right posterior suprahepatic area than of the right infrahepatic area and that a pathologic process of the liver and biliary passage is more often followed by involvement of the right infrahepatic area than of the right posterior suprahepatic area. Taking this into consideration and the percentage of cases presented in which the abscess originates from a lesion in these organs, one sees that in Ochsner and Graves' cases the right posterior suprahepatic area should be involved more often than the right infrahepatic area and the right infrahepatic area more frequently than the right posterior suprahepatic area. Thus, any group of cases will give statistical results which are dependent generally on the proportion in which these three groups of sources are represented.

A subphrenic abscess secondary to appendicitis may first be located in the right infrahepatic area, as Cokkins suggested, and then extend up to the right posterior suprahepatic area, and at this time necessitate operation. Evidence of subsiding infection of the infrahepatic area following appendectomy, with activity in the right posterior suprahepatic area, was found in 3 (3.3 per cent) of the cases in the present series in which operation was performed. It is therefore the source and the time after onset at which the patient is seen which will ultimately determine the location of the infection.

CLINICAL MANIFESTATIONS

The multiplicity and variety of complaints usually attending a subphrenic abscess make it difficult to present a classic picture of the condition. A difference in etiology, age of the patient, location of the abscess and duration of the illness will help to alter the clinical picture. Regardless of the factors influencing the origin of a subphrenic abscess, the mode of onset will always take one of three characteristic forms: (1) sudden, (2) insidious or (3) postoperative.

Sudden Onset.—When the abscess is of sudden onset it simulates a perforated peptic ulcer (more commonly a gastric) with generalized peritonitis. There is a sudden pain in the epigastrium, vomiting, prostration, difficulty in taking a deep breath, a sensation of fulness in

the upper part of the abdomen and tenderness in the epigastric region. Later, signs and symptoms of infection become manifest, with the formation of an indefinite mass in or near the epigastrium. The onset was sudden in 15 per cent of the cases in the present series.

Insidious Onset.—When the onset is insidious, the symptom complex is subacute and simulates that of a chronic obscure intra-abdominal lesion, such as chronic appendicitis of long duration, and gives rise to a retroperitoneal extension of the infection to the subdiaphragmatic area. At first, the symptoms are those of vague aches and pains followed by discomfort in the lower part of the chest posteriorly or in the right flank, with radiation up to the right shoulder. Occasionally, the pain radiates anteriorly to the infrahepatic region. The pain is aggravated by deep breathing. Signs and symptoms of an infection soon become manifest, with gradual elevation of pulse and temperature, as localization occurs. The onset was insidious in 30 per cent of the cases in the present series.

Postoperative Onset.—By far the greatest number of subphrenic abscesses appear postoperatively as a continuation of systemic manifestations, in spite of adequate care given to an intra-abdominal suppurative process. Frequently the subphrenic area is involved at the time of the surgical intervention, but the process is not clinically manifest. In other cases it is directly due to the operation itself. If after an abdominal operation for a suppurative process the immediate or late postoperative course is not smooth, even if weeks have elapsed, and no other satisfactory explanation can be given for the unusual course, a subphrenic collection should be suspected until it is ruled out. The onset occurred after operation in 55 per cent of the cases in the present series.

Regardless of whether the onset is insidious, sudden or postoperative, the symptom complex is more or less the same, the only difference being the acuteness of the clinical course. Clinically, one cannot tell which area a subphrenic abscess occupies. It is for this reason that Piquand [9] classified subphrenic abscesses presenting signs of abdominal involvement as infrahepatic, those presenting signs of thoracic involvement as suprahepatic and those presenting signs referable to the lumbar region as retroperitoneal. A subphrenic abscess is generally not confined to one specific area but may overlap an adjacent one. It will therefore manifest itself clinically by a variable combination of signs and symptoms of involvement of the abdominal, thoracic and lumbar regions, depending on the location of the abscess, the acuteness of the onset, the size of the abscess and whether or not it contains gas. Wahby reported finding gas in 32 of 59 cases from the St. George Hospital. In the present series of cases gas was found in 34 per cent.

General or Systemic Manifestations.—The onset may be vague, with malaise, fatigue, loss of appetite and pallor, accompanied by a dull ache in the region of the abscess. As the condition progresses, the temperature and pulse become elevated and fluctuant. The patient has chills and sweats profusely. Nausea and vomiting usually have made their appearance before this stage, if the lesion is intraperitoneal, and particularly if the onset is acute. As the condition advances, the patient loses weight and complains of pain in the corresponding shoulder and in the region of the abscess, and occasionally hiccups or belching develops. At times there are associated jaundice and severe anemia. The white blood count rises to about 22,000, with 85 per cent polymorphonuclear leukocytes. On examination one finds an acutely sick patient with a hectic flush, a warm moist skin, a short hacking cough, an anxious expression, dyspnea and breathing restricted on one side. There may also be seen a bulging area below the costal margin in the abdomen or bulging edematous interspaces or a mass in the lumbar region.

Examination of the Chest.—During respiration that side of the chest which is involved moves little if at all. The interspaces become widened and bulge. There is a tendency to flaring of the wall of the lower part of the chest in the posterior axillary area. If the abscess is deeply placed, there is retraction of the interspaces rather than widening. The costal arch is tender to pressure in this area. On percussion, there is impairment over the lower part of the chest, and the diaphragm is elevated and fixed in that position. If the abscess is in the anterior infrahepatic area, there is tenderness along the tenth rib anteriorly. If the abscess is in the right posterior suprahepatic area, there is tenderness along the twelfth rib posteriorly. The breath sounds in the area of impaired percussion are distant or entirely suppressed. Occasionally with partial compression of the lung, one hears transmitted bronchial breath sounds in the upper area of impaired percussion. If the abscess contains gas, signs suggesting pneumothorax may be obtained. A friction rub may be heard at the lower part of the thorax. This is not a pleural rub, as was formerly believed, but is due to the diaphragm rubbing against the inflamed upper surface of the liver. If the abscess is on the left side, the heart will be pushed upward or tilted to the right but will not be displaced to the right. When the abscess is on the left side one occasionally hears a peculiar clicking quality to the second heart sound at the apex. To differentiate between subphrenic abscess and empyema thoracis, it should be noted that in empyema the upper limit of the fluid is concave, whereas in subphrenic abscess it is convex (DaCosta[23]). The onset in 45 per cent of the cases in the present series was referable to the thorax.

23. DaCosta, J. C.: Modern Surgery, General and Operative, Philadelphia, W. B. Saunders Company, 1931.

Examination of the Abdomen.—Since the condition usually begins with discomfort in the upper part of the abdomen, one finds the patient in bed favoring that side. During respiration there is an absence of movement of the abdominal wall of the affected side. At times there is a visible mass in the epigastrium, and the skin over it is edematous and discolored. On palpation, the rectus muscle on that side is found to be spastic, and on deep palpation one can feel an indefinite, tender, fixed mass. If the abscess is suprahepatic, the liver is generally pushed downward. On percussion, the area of liver dulness is enlarged downward, and if the abscess contains gas there will be four distinct zones of altered note. From above downward, they are: (*a*) a zone of normal resonance or hyperresonance in the lung, (*b*) a zone of pleural effusion or compression of the lung with dulness, (*c*) a zone of resonance or tympany due to gas and (*d*) a zone of dulness due to the abscess itself.

The onset in 70 per cent of the cases in the present series was with symptoms referable to the abdomen.

Examination of the Lumbar Region.—There is a mass extending out from below the costal margin, posteriorly. It is tender, usually tense and fluctuates deeply. Bogart [24] has pointed out that there is a spasm of the quadratus lumborum muscle on the affected side, which at times will cause scoliosis on that side. The mass may be so large that it reaches around to the axillary line. It is dull to percussion except when it contains gas, and then it will be hyperresonant. Pressure on the mass will cause pain locally and at times it will be referred to the shoulder or epigastrium or to the anterior infrahepatic region on that side. The onset in 25 per cent of the cases in the present series was with symptoms referable to the lumbar region.

Roentgenographic Examination.—On fluoroscopic examination the diaphragm is found to be elevated and flattened at its dome and with the patient in the erect position it moves little during respiration. Underneath the diaphragm and above the liver there is a dense shadow or a gas bubble, below which there is a collection of fluid. Dexter [25] expressed the belief that the loss of diaphragmatic motion is almost pathognomonic of the condition. He also stated that other conditions below the diaphragm will limit the motion of the diaphragm but will not completely inhibit its motion.

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24. Bogart, L. M.: Subphrenic (Subdiaphragmatic) Abscess, Am. J. Surg. **26**:467, 1934.

25. Dexter, R.: Observations on the Diagnosis of Subphrenic Abscess, Am. J. M. Sc. **170**:810, 1925.

LeWald,[26] Pancoast [27] and Granger [28] have shown that by far the greatest single aid in helping to make a diagnosis of subphrenic abscess is a series of well taken roentgenograms. These should be taken in all directions—anteriorly, laterally, obliquely and posteriorly. They should be taken with the patient in the erect and in the prone position and during inspiration and expiration. In the presence of a subdiaphragmatic collection, such plates will show the elevated motionless diaphragm, a small amount of fluid in the costophrenic sinus and the heart pushed up or tilted to the opposite side. Underneath the diaphragm there is a dense shadow or a gas bubble, which at times is above a distinct fluid level. Frequently only a few of these findings are present; however, there are sufficient to make one highly suspicious of a subphrenic collection, but a pleural effusion cannot be ruled out. In such cases Lilienthal suggested pneumoperitoneum to outline the area between the liver and the diaphragm, thereby helping to localize the site of the collection.

An early subphrenic abscess produces a somewhat ill defined clinical picture, which, with the past history and roentgenographic studies, should not be difficult to recognize. That the diagnosis will be overlooked if it is not kept in mind is shown by Overholt's [29] case, in which the diagnosis was not made until six months had elapsed, and by Lockwood's [30] case, in which the diagnosis was not made until twenty months after the onset. In the present series of cases there were 18 (16.2 per cent) in which the diagnosis was not made until four or more months after the onset. In one of these cases seven years had elapsed before the diagnosis was made. In another one of the cases, three months after an appendectomy for a ruptured retrocecal appendix the patient was readmitted to the hospital with vague, persistent pain in the right side of the upper part of the abdomen. A diagnosis of chronic cholecystitis was made, and the gallbladder was removed. Before the operation, a roentgogram of the chest showed the diaphragm to be high on the right side. After operation the position of the diaphragm was unchanged, and the patient stated that she "felt worse

26. LeWald, L. T.: Subphrenic Abscess and Its Differential Diagnosis Roentgenologically Considered, Arch. Surg. **10**:544 (Jan.) 1925.

27. Pancoast, H. K.: The Roentgenological Diagnosis of Liver Abscess With or Without Subdiaphragmatic Abscess, Am. J. Roentgenol. **16**:303, 1926.

28. Granger, A.: Radiological Signs of Subdiaphragmatic Abscess, New Orleans M. & S. J. **82**:748, 1930.

29. Overholt, R. H.: Subphrenic Abscess with Extension into the Right Lung and Cure by Phrenic Exeresis, S. Clin. North America **12**:619, 1932.

30. Lockwood, A. L.: Subdiaphragmatic Abscess, Surg., Gynec. & Obst. **33**: 502, 1921.

than before the operation." However, she was discharged "improved," only to return four months later with a huge retroperitoneal subphrenic abscess. Because of the vague onset and insidious course, seven months had elapsed before the diagnosis was made.

Aspiration.—One frequently reads of aspiration as a diagnostic aid. I believe that this procedure should never be attempted unless it is done at the time of the operation. Weir,[31] as early as 1892 stated: "Negative results often suggest surgical delay, and its chance of help in cases where help is needed as in small collections of pus, and where other symptoms are sufficiently present to determine a course of action, is a very slight one." Ochsner,[11a] citing Hirsch's case, stated that twenty-four attempts at aspiration were made before pus was obtained. Barnard [8] reported a case of transpleural aspiration of an abscess, with death from collapse in three hours. If aspiration fails to reveal pus, it certainly does not rule out its presence.

COMPLICATIONS

While the condition under consideration is rarely primary and is in itself a complication, because of the devastating effects of its sequelae one may logically consider it as primary and its sequelae as complications. Complications following subphrenic abscess will depend on: (1) the acuteness of the onset and the rapidity of spread of the infection producing the abscess; (2) the degree of peritoneal soiling on removal or drainage of a suppurative process; (3) the duration of the subphrenic abscess before its recognition, and (4) the adequacy of surgical care of the subphrenic abscess.

The complications of subphrenic abscess are as follows:

(*a*) Systemic complications. These consist of (1) sepsis and (2) cachexia.

(*b*) Abdominal complications. These consist of (1) rupture of the abscess through the skin, (2) rupture of the abscess into the peritoneal cavity, thereby producing peritonitis, and (3) rupture of the abscess into one of the viscera—the stomach, colon, etc.

In the cases reported here it has frequently been impossible to tell whether a so-called complication was not coexistent with the subphrenic abscess at the time of the diagnosis of the latter or whether the cause of the subphrenic abscess was the same as that of the other abdominal complications. It is my impression that abdominal complications following subphrenic abscess are less common than is generally supposed.

(*c*) Thoracic complications. These consist of (1) pleural effusion, (2) empyema, (3) bronchopleural fistula, (4) abscess of the lung,

31. Weir, A. F.: Remarks on Subdiaphragmatic and Rectal Abscesses of Appendiceal Origin, M. Rec. **41**:173 (Feb. 13) 1892.

(5) pneumonia or pneumonitis, (6) pericarditis, (7) mediastinal abscess, (8) pneumothorax or pyopneumothorax and (9) perforation of the abdomen.

1. Pleural effusion is variously estimated to be present in from 9 to 100 per cent of cases. It was a complication in 30 (36 per cent) of the cases in the present series.

2. Empyema may develop as a later complication of pleural effusion or as a direct infection of the pleural space. Organisms may enter the pleural space either through the lymphatics from below the diaphragm or by a subphrenic abscess rupturing into the pleural space; or empyema may develop in a patient with a subphrenic abscess in whom an abscess of the lung, pneumonia or sepsis is developing as a secondary condition. Empyema following a subphrenic abscess has been variously estimated as occurring in from 11.9 to 42.5 per cent of cases. It was found in 16 (19.2 per cent) of the cases in the present series.

3. Bronchopleural fistula per se does not occur. It is usually secondary to empyema, pneumonia or abscess of the lung. Bronchopleural fistula secondary to subphrenic abscess and its sequelae has been variously estimated to occur in from 5 to 20 per cent of cases. It was found in 4 (4.7 per cent) of the cases in the present series.

4. Abscess of the lung is usually the result of a lymphatic extension into the lung, postpneumonic or embolic in origin. Abscess of the lung following a subphrenic abscess has been variously estimated as occurring in from 6 to 16 per cent of cases. It was found in 8 (9.6 per cent) of the cases in the present series.

5. Pneumonia or pneumonitis is either a superimposed infection or an extension of the process from below the diaphragm to the lung. The incidence of pneumonitis following subphrenic abscess has been variously reported as being from 5.9 to 33.3 per cent. It was found in 10 (12 per cent) of the cases in the present series.

6. Pericarditis is usually the result of a lymphatic extension of the infection from below the diaphragm, especially on the left side, or from empyema, pneumonitis or abscess of the lung. The incidence of pericarditis following subphrenic abscess has been variously reported as being from 6 to 20 per cent. It was found in 2 (2.4 per cent) of the cases in the present series.

7. Mediastinal abscess may result from the breakdown of infected mediastinal glands or as a direct extension into the mediastinum from a subdiaphragmatic abscess, or from pneumonitis, which in turn is due to a subdiaphragmatic abscess. The incidence of mediastinal abscess following subphrenic abscess has been variously reported as being from 2.9 to 7 per cent. It was not seen in the present series of cases.

8. Pneumothorax or pyopneumothorax is the result of a spontaneous rupture of the lung due to any of its causes, or to infection of the pleural space with a gas-producing organism or to a sinus tract extending from below the diaphragm to the pleural space. The incidence of pneumothorax and pyopneumothorax following subphrenic abscess has been variously reported as being from 10 to 30 per cent. It was found in 8 (9.6 per cent) of the cases in the present series.

9. Perforation of the diaphragm may be the result of a pathologic process above or below the diaphragm. The incidence of diaphragmatic perforation following subphrenic abscess has been reported as being from 5 to 49 per cent. It was seen in 7 (8.4 per cent) of the cases in the present series.

General Summary of Thoracic Complications.—In the series of 111 cases studied here there were 85 intrathoracic complications in 68 different patients. Fifty-four (79.4 per cent) showed 1 intrathoracic complication, 11 (16.2 per cent) had 2 intrathoracic complications and 3 (4.4 per cent) had 3 coexisting intrathoracic complications. It was found that intrathoracic complications were usually due to: (1) neglect of the primary cause, (2) failure to make an early diagnosis of subphrenic abscess and (3) an early diagnosis but inadequate surgical care of the subphrenic abscess. Occasionally, one's attention is first called to the subphrenic abscess by the presence of thoracic complications. This occurred in 8 cases (9.6 per cent) in this series. In 2 of the cases there were small perforations of the stomach and in 6, low grade appendical infections.

PROGNOSIS AND MORTALITY

In all cases of subphrenic abscess the prognosis should be guarded. However, the prognosis is more favorable in those cases in which the diagnosis is made early, in which adequate drainage has been established and in which there is freedom from intrathoracic complications. Conversely, the prognosis becomes poorer when the diagnosis is not made until late, when the drainage of the abscess is inadequate and when there are intrathoracic complications. Delay in the institution of what would otherwise have been adequate therapy will often produce poor results. The mortality is greatest in those cases in which pulmonary complications develop. In the presence of intrathoracic complications the mortality in this study was 32.4 per cent—a total of 22 deaths. Beye,[32] studying intrathoracic complications following subphrenic abscess, reported a mortality of 43.5 per cent.

The mortality for subphrenic abscess has been variously estimated from 38 per cent in the cases in which operation was performed (Gate-

32. Beye, H. L.: Thoracic Complications of Subdiaphragmatic Infection, J. Thoracic Surg. **1**:655, 1932.

wood) to 100 per cent in those in which it was not performed (Deaver). With the newer conception of the management of a subphrenic abscess, the mortality has dropped to about 25 per cent. Even this mortality is too high but is in part due to surgically uncontrollable factors, such as preoperative peritonitis, ruptured appendix, perforated peptic ulcer, etc. In the series of 111 cases studied there were 24 deaths, or a total mortality of 21.6 per cent. In the 90 cases in which operation was performed there were 16 deaths, or a mortality of 17.6 per cent. In the 21 cases in which operation was not performed there were 8 deaths, or a mortality of 38.4 per cent.

It is universally agreed that all things being equal, the highest mortality is obtained in transperitoneal drainage of a subphrenic abscess and the lowest, in extraperitoneal drainage of the abscess. The mortality is distinctly lower in those cases in which drainage has been instituted without contamination of a serous cavity. In the present series of cases the mortality for those in which extraperitoneal drainage was instituted (71 cases) was 8.5 per cent whereas for those cases (7) in which transpleural drainage was instituted it was 42.6 per cent and for those (12) in which transperitoneal drainage was used it was 58.1 per cent. In Ochsner and Graves'[1] series of cases collected from the literature, the mortality from extraperitoneal drainage was 21 per cent, that from transpleural drainage was 39 per cent and that from transperitoneal drainage was 35.5 per cent. The mortality in all patients between the ages of 20 and 50 years was highest. In this study the mortality for the group of patients below 20 years of age was 15 per cent, that for the group between the ages of 20 and 50 years, 65 per cent, and that for the group between the ages of 50 and 70 years, 20 per cent. Barnard[8] reported similar mortalities on the basis of age.

TREATMENT

The treatment may be considered under: (*a*) prophylaxis, (*b*) conservative care and (*c*) operation.

Prophylaxis.—A considerable number of subphrenic abscesses subside spontaneously. Therefore, efforts should be directed toward accomplishing this end, and at the same time an effort should be made to decrease the severity of those abscesses which occur in spite of prophylactic care. Prophylaxis begins with the early institution of surgical care for a suppurative process or for a perforated viscus. In the operating room it consists of carefully walling off the pathologic area, so as to avoid the spread of infectious material, and, similarly, careful handling of the viscera, so as to avoid squeezing infectious material out of them, and, finally, the avoidance of traumatization while removing an offending cause. At the termination of the surgical procedure

dependent drainage is required in every suppurative process, especially in those cases in which there is peritoneal contamination. The present tendency of allowing the infection to localize in cases of ruptured appendix before surgical intervention should be condemned as inviting the formation of subphrenic abscesses. Postoperatively, prophylaxis consists of placing the patient with a ruptured ulcer or peritonitis in the Fowler position as soon as feasible. Coffey has shown that to drain the flanks into the pelvis the body must be tilted to an angle of about 60 degrees. The use of fluids in large quantities are advocated "to wash away the toxins." In those cases in which there is increased toxicity, a blood transfusion is often of help in tiding the patient over a stormy course.

Conservative Care.—For an abscess in the early stage, watchful waiting is perhaps the best procedure. The patient should be kept in bed in the Fowler position. The lower part of the chest on the affected side should be strapped tightly to inhibit the suction effect of the diaphragm. Dry heat should be applied locally. With these measures, general supportive care should be instituted and a transfusion of blood given as frequently as indicated. These measures should be continued as long as the patient improves. If the patient fails to respond, or if the response is not satisfactory, surgical intervention should be instituted at once.

Operation.—The first principle in surgical treatment, that is, "where there is pus, let it out," holds good here as elsewhere in the body. As a corollary to this principle, one may add: "Seek dependent drainage without spreading the infection." This principle is axiomatic in handling subphrenic abscesses.

The surgical approach to a subphrenic abscess may be: (1) transserous, i. e., transpleural or transperitoneal, or (2) extraserous, i. e., extrapleural or extraperitoneal.

1. The transserous route is by far the easiest technical approach to a subphrenic abscess and as a result "surgeons have adhered to it slavishly in spite of a high mortality." To drain an infected area via an uninvolved serous cavity is not sound surgically. The mortality following transpleural and transperitoneal drainage is approximately 50 per cent—a mortality that is frightfully high. The method should therefore be abandoned in favor of a method which is surgically sound and which carries with it a mortality which is considerably less.

2. For the extraserous route, either the extrapleural approach or the extraperitoneal approach may be used.

The extrapleural approach is more difficult than the extraperitoneal and carries with it the danger of opening the costophrenic angle as the pleura is being stripped away from the diaphragm.

The extraperitoneal approach is recommended as the method of choice, because the peritoneum is more readily separated from the diaphragm than from the pleura. This approach may be made either anteriorly or posteriorly.

The posterior extraperitoneal approach (on the right side) is illustrated in figures 3, 4 and 5.

A description of the technic follows:

The patient lies on the uninvolved side, with the lower part of the chest raised by a kidney rest, so that the lower dorsal portion of the spine is convex upward. The legs are drawn up and flexed on the abdomen, and the body is inclined slightly forward. Local or paravertebral block anesthesia is used. A transverse incision is made at the level of the middle of the first lumbar vertebra, beginning in the

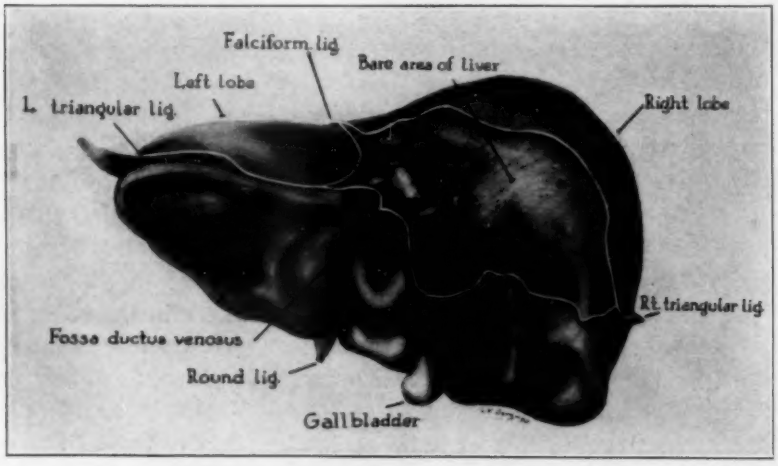

Fig. 3.—The liver seen from behind and partly rotated forward to expose the upper posterior surface and part of the inferior surface. This view also shows the peritoneal reflections and ligamentous attachments of the liver and the bare area of the liver.

posterior axillary line, and is carried backward to the paravertebral area. The twelfth rib is exposed and resected subperiosteally. The erector spinae muscles are retracted medially without cutting them. The original incision is then carried deeply through the bed of the twelfth rib, thereby avoiding the costophrenic angle and the pleura. The spinal attachments of the diaphragm at this level are severed, and the perinephric fascia is exposed. This fascia is gently pushed inward and downward, as is the kidney, until the lower edge of the liver is felt. This exposes the right infrahepatic area and the peritoneum. The infrahepatic area is palpated for induration. If present, the area is aspirated. If pus is obtained, the area is opened by means of the exploring finger. If no pus is obtained the peritoneum on the inferior surface of the diaphragm is gently pushed away until the region about the right posterior suprahepatic area is reached. Before the abscess is reached, an area of induration will be palpable. This area is aspirated, and if pus is present the finger is manipulated into the abscess. A large black rubber

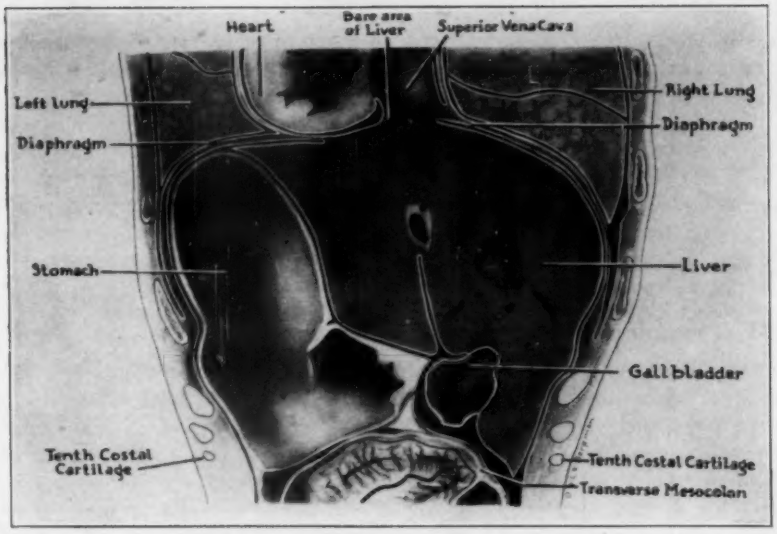

Fig. 4.—Coronal section through the middle of the body, as seen from behind, showing the subphrenic area, the diaphragm and the transverse mesocolon. It also shows the relationship of the peritoneal cavity to the pleural cavity at the costo-phrenic sinus.

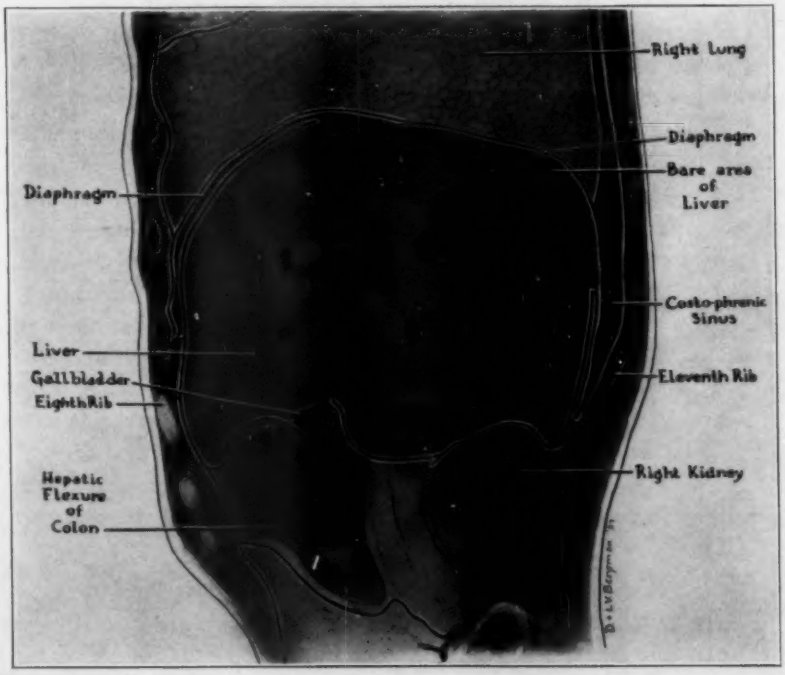

Fig. 5.—Sagittal section through the right renal region, showing the relations of the subphrenic area to the surrounding structures. It also shows the relationship of the pleural space to the peritoneal cavity.

drainage tube, with a cigaret drain on either side of it, is inserted into the abscess cavity and exteriorized through the wound in the skin, to which all three are fixed. If no pus is obtained on aspiration, the subdiaphragmatic peritoneum is further decollated until the extraperitoneal area is reached. This area is aspirated, and if pus is obtained the abscess is treated as suggested previously. Through this incision, the right infrahepatic and the right posterior suprahepatic intraperitoneal areas and the right posterior extraperitoneal area may be reached and drained. Considering that this procedure will reach about 65 per cent of the subphrenic abscesses, it cannot be too highly recommended. On the left side the best approach is via the left posterior infrahepatic area.

The technic for the anterior extraperitoneal approach follows:

An incision is made below the costal margin and parallel to it, on the affected side. The tissues are separated down to the parietal peritoneum. By finger dissection the peritoneum is mobilized from the inferior surface of the diaphragm until an indurated area is felt. This is aspirated, and if pus is obtained, the finger is gently pushed into the area. The pus is then evacuated, and the abscess cavity is drained in the manner previously described. The anterior extraperitoneal approach is a good one, and for those abscesses localized in the right anterior suprahepatic area and the right infrahepatic area it will best meet the surgeon's requirements. On the left side it is ideal for collections of pus in the anterior infrahepatic and suprahepatic areas, as well as a good approach for the infections of the anterior extraperitoneal area.

Occasionally, an intraperitoneal abscess becomes adherent to the parietal peritoneum, and localization takes place under it, with local obliteration of the peritoneal space. In such instances one is at liberty to open the abscess and drain it in the usual manner employed for any localized abscess. The local reaction has sealed off the peritoneum, preventing its contamination.

In those cases in which there is a coexisting empyema, drainage via the extraperitoneal route is contraindicated. In all likelihood the diaphragm is perforated, and therefore thoracotomy should be done, the opening in the chest being made large enough to allow exploration of the diaphragm. The diaphragm is explored, and if the perforation is found, the subphrenic abscess and the empyema are drained, separate drains being employed. If the abscess is not found and one is certain that a subphrenic abscess is present, the diaphragm is nicked in the direction of its fibers, over the site of the abscess. A black rubber drain is inserted into the abscess cavity and exteriorized with the empyema tube through the wall of the chest, to which the tubes are fixed.

SUMMARY AND CONCLUSIONS

I have endeavored to present a general résumé of the etiology, course and treatment of subphrenic abscess, together with a review of 111 cases. I advocate surgical intervention suited to the conditions present and feel that the extraperitoneal route is the ideal one in most types of

subphrenic abscess. When this approach is used as indicated it will generally lead to prompt recovery. With the more general use of this approach I find from the statistics at the Jewish Hospital and from those reported by other authors that the apalling mortality usually encountered in subphrenic abscesses is considerably lowered. In the past ten years the mortality at the Jewish Hospital following operation by the low extraperitoneal route was 7.1 per cent, whereas in this same period that following operation by the transserous route was 52.5 per cent.

135 Eastern Parkway.

TREATMENT OF TUMOR OF THE PAROTID GLAND

SURVEY OF THE RESULTS OBTAINED AT THE BARNARD FREE SKIN AND CANCER HOSPITAL

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The present status regarding the etiology of tumor of the parotid gland, which for many years was the subject of a lively academic discussion, has been summarized by Ewing [1] as follows:

1. The endothelial origin has been disproved.

2. No single source of mixed tumor meets all requirements. Some are distinctly adenomatous and probably arise from the acini and the ducts of the gland in which they are well incorporated. Others are encapsulated or extraglandular, and take the form of basal cell or adenocystic epithelioma. These probably arise from misplaced and occasionally embryonal portions of gland tissue. Branchial remnants may possibly be connected with this group.

3. The derivation of mucous tissue and cartilage from gland epithelium has been satisfactorily proved, and there is no necessity of including in the originating tissue any cartilaginous structures.

McFarland,[2] reporting a series of ninety cases of tumor of the parotid gland in 1926, differed somewhat from Ewing in that he expressed the belief that the theory of enclavement or embryonal sequestration affords the most satisfactory explanation of the origin of this type of tumor. He also stated that the tumor has no relationship to the normal structures in which it occurs but from which it does not arise.

That the majority of mixed tumors are benign and if completely removed do not tend to recur is conceded by nearly all authorities. However, if a tumor does recur it may become progressively more invasive without giving rise to distant metastases and may cause the death of the patient. The problem of malignant change in a simple mixed tumor does not have the universal support that the concept of the simple mixed tumor itself possesses. Some investigators believe that there is a certain percentage of simple mixed tumors which undergoes malignant degeneration.

From the Surgical Service of Dr. William E. Leighton.

1. Ewing, J.: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 775.

2. McFarland, Joseph: Ninety Tumors of the Parotid Region, Am. J. M. Sc. **172**:804, 1926.

Blair and Olch [3] stated that malignant degeneration is not a separate clinical entity but a distinctly secondary change which occurs in a mixed tumor which has been present for years in a benign state. This change occurs, they stated, during the so-called "cancer age," and although its etiology is unknown in many instances it is thought to be due to traumatism, such as massage or attempted removal. Blair and Olch quoted Wood as stating that 25 per cent of mixed tumors show this change. They also quoted Kuttner, who stated that 28 per cent show this change.

Kenna,[4] reporting a series of 137 cases of tumor of the salivary glands, stated that 35 per cent of cancers in his series arose from the degeneration of a mixed tumor.

McFarland, in his first study, stated that malignant change in a mixed tumor must be rare and its occurrence difficult to prove. Stout,[5] in a report in 1927, expressed the same opinion. In a later study in 1933 McFarland [6] supplemented his earlier paper, stating that these tumors are malignant in themselves and not by virtue of any sarcomatous or carcinomatous degeneration.

Benedict and Meigs,[7] reporting a series of 225 cases of tumor of the parotid gland, concluded that surgical intervention is the treatment of choice, and in the case of a malignant tumor they advised early and complete radical operation.

Sistrunk [8] reported that surgical treatment has given excellent results in cases of mixed tumor.

Geschickter and Stein [9] reported 241 cases of tumor of the parotid gland in 1934 from the Johns Hopkins Hospital and stated that both surgical intervention and irradiation have their place in the treatment of such growths. They stated that a small benign tumor is best treated by complete excision with the knife, whereas a malignant tumor, in their experience, is best treated by irradiation first and then by excision if it becomes operable.

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3. Blair, V. P., and Olch, I. Y., in Lewis, Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, 1930, vol. 4, chap. 5, p. 21.

4. Kenna, R.: Tumors of the Salivary Glands with Their After History, Brit. J. Surg. **9**:76, 1921.

5. Stout, A. P.: Human Cancer, Philadelphia, Lea & Febiger, 1932, pp. 70-71.

6. McFarland, Joseph: Tumors of the Parotid: Studies of One Hundred and Thirty-Five Cases, Surg., Gynec. & Obst. **57**:104, 1933.

7. Benedict, E. B., and Meigs, J. V.: Tumors of Parotid Gland: Study of Two Hundred and Twenty-Five Cases with Complete End Results in Eighty Cases, Surg., Gynec. & Obst. **51**:626, 1930.

8. Sistrunk, Walter: Tumor of the Parotid Gland, S. Clin. North America **1**:1515, 1921.

9. Stein, I., and Geschickter, C. F.: Tumors of the Parotid Gland, Arch. Surg. **28**:492 (March) 1934.

Wood [10] recommended surgical intervention as the proper treatment and advised that it be done early. Most failures, he asserted, are due to the complicating anatomic relationship of the facial nerve.

Jackson [11] concurred in recommending early operation in cases of mixed tumor.

Blair and Olch advised early removal of a tumor of the parotid gland together with a portion of the normal gland superficial to the facial nerve.

McFarland, in his report of 1933, drew some rather pessimistic conclusions regarding treatment. Except for improvement in appearance or to ease the patient's mind, he stated that it would be just as well not to operate. He differed from other observers in that he cautioned against the removal of small tumors, as he considered that they are likely to recur. Operation, he stated, has done little for the malignant tumor of the parotid gland, while irradiation is of no benefit. If operation is decided on, he stated that there is no hurry and that due consideration should be given the possible accidents, namely, facial paralysis and salivary fistula.

The role played by irradiation in the treatment of a tumor of the gland is at present a matter of controversy. Benedict and Meigs stated that in their series roentgen and radium therapy have been beneficial as a palliative measure only. Geschickter and Stein also reported that irradiation is beneficial as a palliative measure in cases of malignant tumor. They also applied irradiation postoperatively to the bed of the tumor.

Merritt [12] stated that the treatment of a mixed tumor is largely in the hands of the radiologist and that although a small tumor may be excised, radium will accomplish the same results. He further stated that a combination of irradiation and surgical treatment is illogical; if one is sufficient, the other is superfluous.

Widman,[13] reporting his results in 54 cases of tumor of the parotid gland, of which 35 were malignant and 19 were benign, stated that the roentgen rays have shown no appreciable effect on clinically benign tumors. No clinical cures have been obtained in 27 cases of advanced primary and recurrent inoperable malignant tumors. The palliative effect of the roentgen rays and radium were sufficient to justify recommending them for this purpose.

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10. Wood, Francis C., in Nelson Loose Leaf Living Surgery, New York, Thomas Nelson & Sons, 1927, vol. 2, p. 112.

11. Jackson, A. S.: Mixed Tumors of the Parotid Gland, Wisconsin M. J. **31**:701, 1932.

12. Merritt, E. A.: Mixed Tumors of the Parotid Gland, Am. J. Roentgenol. **25**:507, 1931.

13. Widman, B. F.: The Treatment of Parotid Tumors with Roentgen Rays and Radium, J. M. Soc. New Jersey **31**:95, 1934.

William Neill,[14] who reported 71 cases of tumor of the parotid gland, stated that the combination of surgical treatment and irradiation for small tumors and irradiation alone for larger tumors is most effective.

ANALYSIS OF CASES

In a twenty-four year period preceding July 1, 1936, 65,351 patients have been admitted to the Barnard Free Skin and Cancer Hospital, in all departments. Seventy of this number had growths diagnosed as tumor of the parotid gland, 34 being mixed tumors and 36 malignant tumors. Eighteen of those with mixed tumors received treatment, and the diagnosis was confirmed by examination of tissue, while 16 did not receive treatment, and the diagnosis was made merely by clinical examination. In the latter class, treatment was usually refused by the patient because of possible injury to the seventh nerve.

There were more females with mixed tumors than males, the proportion being 25:9, or 73.5 per cent females and 26.4 per cent males. Twenty-three of the mixed tumors occurred on the right side, while 11 were on the left. The age span of the patients with mixed tumor was a wide one, varying from 15 to 74 years, with an average of 47.31 years. Duration of the tumors varied from a short period of two months to forty-two years, with an average duration of eleven and two one-hundredths years, showing evidence of a fairly slow rate of growth. The reason for seeking treatment was not elicited for the series.

In discussing treatment with the patient, the possibility of injury to the seventh nerve is usually pointed out, and it is felt that this, perhaps more than any other factor, accounts for the patient's refusal of treatment. Eighteen patients with mixed tumors were treated; 14 were subjected to simple excision of the mass, it being either shelled out with its capsule or excised with a portion of healthy gland tissue on all sides. Four of the patients were not followed, while 10 showed no evidence of recurrence in periods varying from six weeks to nine years. I hesitate calling any of these patients cured, as McFarland stated that the growths may recur up to a period of thirty years. One patient was subjected to what is termed a "radical excision" and died two weeks later while still in the hospital. This, in my opinion, was an "operative death." One patient was subjected to excision by cautery plus the application of radon (20 seeds), and in spite of the fact that the section showed mixed tumor she died six months later from cancer. Another patient was treated with radon seeds alone, and recurrence of the tumor was noted twenty-six days after treatment. However, it must be pointed

14. Neill, W., Jr.: Observations on Seventy-One Mixed Tumors of the Parotid Gland, M. J. & Rec. **136**:187, 1932.

Summary of Data on Mixed Tumors and Malignant Tumors of the Parotid Gland

Type of Tumor	Number of Cases	Number of Tumors Treated	Number in Males	Number in Females	Right Side	Left Side	Not Stated	Average Age, Yr.	Average Duration, Yr.	No Recurrence
Mixed tumors	34	18	9	25	23	11	..	47.32	11.02	10*
Malignant tumors	36	23	22	13	15	19	2	58.33	2.72	6†

SUMMARY OF TREATMENT USED

Types of Treatment Used for Mixed Tumors ‡		Types of Treatment Used for Malignant Tumors		Types of Treatment Used on Tumor Which Did Not Recur ‡	
Simple excision	14	Radical operations	9	Radical operations	2
Radical excision	1	Radical operation plus 1,200 mg. hours radium	1	Local excision	1
Excision by cautery plus 20 radon seeds	1	Local excision	4	Radical operation plus 1,200 mg. hours of radium	1
Radon seeds	1	Cautery excision	1	Excision by cautery	1
Excision and radium element	1	Local excision of gland plus ascending ramus of mandible	1	Local excision plus resection of mandible	1
		Local excision plus cautery to the surface	1		

DATA ON UNTREATED TUMORS

Mixed Tumors					Malignant Tumors				
Date	Age of Patient, Yr.	Sex of Patient	Duration of Tumor	Side	Date	Age of Patient, Yr.	Sex of Patient	Duration of Tumor	Side	Microscopic Diagnosis
5/ 4/31	78	M	8 yr.	R	5/23/32	67	F	4 mo.	R	Carcinoma of parotid gland
2/ 2/32	47	F	5 yr.	L	1/19/22	67	F	6 yr.	R	None
5/15/32	68	M	15 yr.	R	12/16/23	80	M	6 mo.	R	None
5/12/30	38	F	9 yr.	L	2/13/24	62	M	10 yr.	R	None
5/19/26	45	F	13 yr.	L	4/28/24	58	F	2 mo.	R	None
2/26/26	64	F	42 yr.	R	12/28/31	81	M	11 mo.	R	None
10/26/16	67	M	35 yr.	R	1/26/32	51	M	6 yr.	L	None
10/17/30	74	M	18 mo.	L	9/26/11	61	F	3 yr.	R	None
2/16/26	35	F	6 yr.	R	9/15/14	59	F	2 yr.	L	None
5/23/32	67	F	4 mo.	R	1/14/15	53	M	?	?	None
1/29/34	44	F	21 yr.	R	6/20/34	48	F	6 mo.	R	Biopsy; squamous cell carcinoma, grade 3
3/19/34	38	F	10 yr.	R	4/22/35	60	M	5 mo.	L	None
5/ 8/35	48	F	20 yr.	R	10/16/35	55	F	2 mo.	L	None
2/24/36	72	M	2 mo.	L						
4/ 6/36	49	F	6 mo.	R						
4/24/36	47	F	2 yr.	R						

DATA ON TREATED TUMORS

Date	Age of Patient, Yr.	Sex of Patient	Duration of Tumor	Side	Treatment	Microscopic Diagnosis	Follow-Up Study
					Malignant Tumors—Surgical Treatment		
11/ 7/32	42	F	6 mo.	R	Radical operation	Malignant mixed tumor with metastasis	12/ 7/34: Recurrence; also cancer of uterus
2/ 2/23	52	M	25 yr.	L	Radical operation	Malignant mixed tumor	7/19/23: Recurrence in flap
12/10/23	59	M	6 mo.	L	Radical operation	Malignant mixed tumor	7/ 6/24: Died of cancer
9/ 8/24	70	M	3 mo.	R	Local excision plus 800 mg. hours of radium	Malignant mixed tumor	1925: Died of cancer
6/15/26	66	M	3 mo.	L	Excision with cautery	Malignant mixed tumor with	

6/15/26	66	M	3 mo.	L	Excision with cautery	Malignant mixed tumor with metastasis	8/12/26: Died
7/25/27	53	M	2 yr.	L	Excision with cautery plus radium	Malignant mixed tumor	2/ 4/31: Died of cancer
8/17/27	58	M	2 yr.	R	Radical operation	Malignant mixed tumor	1/19/34: Recurrence
9/16/29	67	M	7 mo.	L	Radical operation	Malignant mixed tumor	6/15/34: No recurrence
3/ 6/31	31	M	3 mo.	L	Local excision	Malignant mixed tumor	8/19/35: No recurrence
3/18/18	66	F	5 mo.	L	Excision	Malignant mixed tumor	7/26/18: Died
3/23/32	50	M	2 yr.	L	Excision and dissection of neck	Malignant mixed tumor	6/15/32: Metastases to buccal mucosa
10/10/34	46	M	10 yr.	L	Radical operation and dissection of neck with 1,200 mg. hours radium	Malignant mixed tumor	10/18/35: No recurrence
4/24/31	74	M	1 yr.	R	Radical operation	Squamous cell carcinoma, grade 2, with metastases	6/15/35: Died of cancer
9/18/31	79	F	1 mo.	L	Excision with cautery	Squamous cell carcinoma	9/11/35: No recurrence
4/20/36	32	F	1 yr.	R	Radical operation	Malignant mixed tumor	6/12/36: Healed; no recurrence
3/ 2/36	53	M	8 mo.	R	Radical operation	Malignant mixed tumor	3/10/36: Died; pneumonia; operative death
5/25/36	74	F	2 yr.	L	Excision of gland and a portion of ascending ramus of mandible	Squamous cell carcinoma, grade 2	7/20/36: Healed
					Malignant Tumors—Radiation Therapy		
7/30/18	61	M	6 wk.	L	8,250 mg. hours of radium	.....	7/26/18: Died of cancer
19/29/34	67	F	18 mo.	R	900 mg. hours of radium	Carcinoma	12/ 2/34: Ulcer thickening; still present
4/29/19	84	..	.....	..	Record incomplete	.....	9/15/19: Died of cancer
8/19/25	53	M	7 mo.	L	Biopsy and 700 mg. hours of radium	.....	8/ 6/26: Died of cancer
10/18/26	43	M	6 mo.	L	Palliative x-ray therapy	.....	11/ ?/26: Died of cancer
7/18/35	59	M	1 yr.	L	27.6 millicuries of radon	Squamous cell carcinoma, grade 2	1/16/36: Recurrence
					Mixed Tumors		
6/30/30	28	F	12 yr.	R	Enucleation	Mixed tumor	Unable to locate
3/28/27	63	F	40 yr.	R	Excision	Mixed tumor	5/28/30: No recurrence
4/15/26	21	F	7 mo.	L	Excision	Mixed tumor	6/23/32: No recurrence
9/10/23	68	F	4 yr.	R	Excision	Mixed tumor	Sept. 1928: Died from other causes
3/ 7/30	45	F	13 yr.	R	Excision	Mixed tumor	6/11/30: No recurrence
1/28/32	28	F	3 yr.	R	Excision	Mixed tumor	7/21/23: No recurrence
4/29/24	43	F	13 yr.	R	Excision	Mixed tumor	6/ 1/33: No recurrence
9/29/27	49	F	18 yr.	R	Excision with cautery plus 20 radon seeds	Mixed tumor	3/ 6/28: Died of cancer
11/14/27	55	F	14 yr.	L	Excision	Mixed tumor	6/21/33: No recurrence
10/29/28	74	M	3 yr.	R	Radical excision	Mixed tumor	11/11/28: Died after operation
8/ 1/29	35	F	1 yr.	R	20 radon seeds	Mixed tumor	8/27/29: Recurrence
9/22/27	36	F	12 yr.	L	Excision	.....	Unable to locate
8/ 6/15	15	M	18 mo.	R	Excision	.....	Unable to locate
10/29/34	29	F	5 mo.	R	Excision plus 200 mg. hours of radium	Mixed tumor	12/5/34: No recurrence
9/31/34	35	M	10 yr.	L	Excision	Mixed tumor	Unable to locate
3/19/35	36	M	15 yr.	L	Excision	Mixed tumor	10/10/35: No recurrence
9/19/34	34	F	7 yr.	L	Local excision	Mixed tumor	2/ 4/35: No recurrence
2/20/35	39	F	18 yr.	R	Local excision	Mixed tumor	9/24/35: No recurrence

* The period of time noted for "No Recurrence" extends from six weeks to nine years.
† The period of "No Recurrence" extends from seven weeks to fifty-seven months.
‡ One "operative death."

out that this patient had a recurrent tumor when she first came into the clinic. One patient was treated with excision plus 200 mg. hours of radium element, and at the last observation, six weeks after treatment, no recurrence was noted.

Among the patients treated at the hospital "no recurrences" has been reported as soon as six weeks postoperatively, as it is stated that recurrences usually occur immediately. On the other hand, it has been shown that they may occur as late as thirty years, and hence one should hesitate in declaring any patient cured.

There were 36 patients with malignant tumors of the parotid gland noted in the group at the Barnard Hospital. Of these 17 were treated surgically, 6 were treated by radiation and 13 received no treatment of any kind. In the group treated surgically, microscopic sections showed 14 malignant mixed tumors and 3 squamous cell carcinomas. Biopsy was done in only 2 of the 6 cases in which irradiation was employed. However, the diagnoses in the remaining 4 was correct because the patients had recurrences or died of the tumor. Biopsy specimens were obtained from only 2 of the untreated malignant tumors. The age of the patients in this group varied from 31 to 84, with an average of 58.33 years, while the duration of the tumor varied from one month to twenty-five years, with an average of two and seventy-two one-hundredths years. There were 22 males and 13 females in the group, and in 1 case the sex was not stated. Fifteen tumors were located on the right side and 19 on the left. In 2 cases the records did not state on which side the tumor was located. The type of surgical treatment which was used varied. In 9 instances a radical operation was employed, i. e., excision of the entire parotid gland to the pharyngeal wall, together with dissection of the tributary lymphatics of the neck. In 2 of these 9 cases there was no evidence of recurrence in fifty-seven months and two months, respectively. The remainder of the patients have died of the disease or show advanced recurrence. One patient underwent the radical operation, and received in addition 1,200 mg. hours of radium, and when last seen, one year after operation, showed no evidence of recurrence. In 2 instances, local excision was used, once with a knife and once with cautery, and in addition radium was applied to the bed of the tumor. Both patients have since died of tumor. Two patients received local excision alone. One died of the tumor, while the other showed no evidence of recurrence in fifty-three months. One tumor was excised by cautery, with no evidence of recurrence in forty-eight months. In another instance simple excision was used, with the application of the actual cautery to the bed of the tumor. This patient later died of cancer. Local excision of the gland, together with a portion of the ascending ramus of the mandible, was

employed on 1 occasion, and when the patient was last observed, two months after the operation, healing had taken place. There was one "operative death" in this series, a mortality of 5.8 per cent.

No attempt has been made to report cures in this series, as the longest observed period of postoperative freedom from the disease has been fifty-seven months. I merely wish to state that of 17 cases of malignant tumor of the parotid gland in which surgical treatment was given 4 malignant mixed tumors showed no evidence of recurrence in fifty-seven, fifty-three, twelve and two months, respectively, while 2 squamous cell carcinomas showed no evidence of recurrence in forty-eight months and seven weeks, respectively.

SUMMARY

Seventy cases of tumor of the parotid gland were noted in 65,351 patients admitted to the Barnard Free Skin and Cancer Hospital during a twenty-four year period.

There were 34 simple mixed tumors of the parotid gland and 36 malignant tumors.

Eighteen simple mixed tumors of the parotid gland were treated. Ten of the 18 patients showed no evidence of recurrence.

Seventeen of the 36 malignant tumors were treated surgically. Six of the patients are free from recurrence in periods varying from seven weeks to fifty-seven months.

Radiation, except for palliation, has not been effective at the hospital.

The cure of malignant tumor of the parotid gland is extremely difficult.

Dr. William E. Leighton gave valuable assistance in the preparation of this paper.

MECKEL'S DIVERTICULUM

ITS INCIDENCE AND SIGNIFICANCE IN ROUTINE OPERATIONS ON THE ABDOMEN

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A review of the literature on Meckel's diverticulum and a search through the surgical files of the New York Post-Graduate Medical School and Hospital reveal a particular significance to the finding of this congenital anomaly at routine operations on the abdomen—a significance not so striking because of the incidence of the anomaly as in its production of symptoms which mimic those of other acute abdominal conditions. In but comparatively few instances has a diverticulum been the specific surgical indication, and all too frequently the symptom complex of acute diverticulitis has been interpreted in terms of other gastrointestinal conditions.

Since first described by Johann Friedrich Meckel in 1809 [1] and 1812,[2] numerous records of the occurrence of the diverticulum have been made, but it appears to have been encountered in most cases as an incidental finding during laparotomy or at necropsy. This point of view is borne out by recent personal communications from surgeons of large experience who state that an increasing number of diverticula have been found since routine examination of the distal segment of the ileum is being made; in other words, since surgeons have become "diverticulum minded."

EMBRYOLOGY

The (vitelline) omphalomesenteric duct usually begins to atrophy during the early weeks of fetal life and normally should disappear. Complete obliteration, however, may fail anywhere along the course of the duct. Persistence of the proximal segment manifests itself as

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1. Meckel, Johann Friedrich: Ueber die Divertikel am Darmkanal, Arch. f. d. Physiol. **9**:421-453, 1809.

2. Meckel, J. F.: Handbuch der pathologischen Anatomie, Leipzig, C. H. Reclam, 1812, vol. 1, p. 579; cited by Burger.[18] (The original German article was not available at the library of the New York Academy of Medicine, although translations into French, and into English from the French, are obtainable.)

Meckel's diverticulum, its frequency in this country being estimated as anywhere from 0.14 to 3 per cent of the population, with an average of about 2 per cent. Mathews,[3] however, expressed the belief that even 2 per cent is an overestimate but that a good many diverticula are overlooked at operation. On the other hand, autopsy data reported by Adami and Nicholls [4] and by Cunningham [5] show that Meckel's diverticulum was encountered in only 2.7 and 2 per cent of their cases, respectively. These various figures are somewhat lower than those given in Europe, where greater opportunity for postmortem examination prevails.

Although Meckel's diverticulum is found at practically any period of life, in the clinical cases reported the patients are mostly children and young adults. In the series of cases which forms the basis of this article, the age distribution of the patients was of the widest possible range—from infancy to the age of 66. Specifically the patients in this series included 2 children of 6 and 7 months, respectively, and 4 between the ages of 5 and 10 years; 1 patient 15 years of age, and 5 patients in the third decade, 4 in the fourth, 3 in the fifth, 1 in the sixth and 3 in the seventh decade. (In the last group 2 were 62 years of age and 1 was 66.) Collected statistics in regard to sex showed a preponderance in the males, the ratio being 4:1, 3:1 or 2:1. Greenblatt, Pund and Chaney,[6] however, in a series of 18 cases recently reported a preponderance of females in the ratio of 3:2.

ANATOMY

Meckel's diverticulum is extremely variable in its anatomy. It may be represented by a mere cupola-like outpouching of the small intestine, or it may be a projection 12 inches (30 cm.) or more in length, while the average diverticulum is approximately the size of a finger, with its end rounded, split or lobulated. Its shape may be conical, bulbous or even spherical from constriction at its base. Its usual point of origin is opposite the mesentery of the bowel, but its attachment may be lateral or even intramesenteric. It may or may not have a well defined mesentery of its own. The site of the diverticulum is usually the lower portion of the ileum, from 12 to 36 inches (30 to 90 cm.) proximal

3. Mathews, Frank S.: Meckel's Diverticulum: A Report of Twelve Cases Including One Tumor, Arch. Surg. **10**:720-729 (March) 1925.

4. Adami, J. G., and Nicholls, A. G.: Principles of Pathology, ed. 2, London, H. Frowde, 1911, vol. 2, p. 427.

5. Cunningham, D. J.: Manual of Practical Anatomy, ed. 8, revised and edited by Arthur Robinson, New York, William Wood & Company, 1930, vol. 2, p. 312.

6. Greenblatt, Robert B.; Pund, Edgar R., and Chaney, Ralph: Meckel's Diverticulum: An Analysis of Eighteen Cases with Report of One Tumor, Am. J. Surg. **31**:285-293, 1936.

to the ileocecal junction, its exact location depending on variations in the development of the limbs of the umbilical flexure of the midgut and on the age of the patient.

Apart from its musculature, which at times is somewhat thin, the structure of the diverticulum is analogous to that of the intestinal wall, even to the existence of Peyer's patches.

HETEROTOPIA

Elements of the gastro-intestinal tract other than mucosa of the small intestine are sometimes present in Meckel's diverticulum. Such elements include gastric and duodenal mucosa and aberrant pancreatic tissue. According to Greenblatt and his co-writers,[6] the presence of heterotopic tissue is estimated as varying from 15 to 25 per cent.

Several theories have been advanced in an attempt to explain the occurrence of this tissue:

Albrecht's theory is based on the pluripotential capacity of the cells lining the omphalomesenteric duct and the primitive intestinal tube to develop into any of the glandular structures in the adult intestine or accessory glands, with the ability to retain one or the other potentiality. This theory would explain the presence of gastric mucosa in Meckel's diverticulum or the occurrence of ectopic pancreatic tissue.

Schaetz's reimplantation or auto-implantation theory reflects an opinion based on experimental observations. He concluded that movements of the maternal organism are communicated to the developing ovum and that fragments of potential gastric mucosa are torn loose and reimplanted at physiologic narrowings in the intestinal tract, one of which is the obliterating omphalomesenteric duct.

Farr and Penke[7] suggested that the vitello-intestinal duct originally may have possessed a digestive function, on the theory that the material in the yolk sac has to be digested. In their series of 13 cases in which operation was performed, gastric mucosa was present in 6 (approximately 50 per cent), while Schaetz found it in only 16 per cent of his autopsy material. These findings, in Farr's opinion, have more than casual significance.

In connection with the foregoing theory, the question has been raised as to whether or not the yolk material really requires digestion in the intraluminal sense, and if so, what type of mucosal epithelium originally lines the yolk stalk. Grosser,[8] in a study of the development

7. Farr, Charles E., and Penke, Madeline: Meckel's Diverticulum, Ann. Surg. **101**:1026-1042, 1935.

8. Grosser, O.: Development of Egg Membranes and Placenta, in Keibel, F., and Mall, F.: Manual of Human Embryology, Philadelphia, J. B. Lippincott Company, 1910, vol. 1, pp. 173-174.

of egg membranes, stated that at the commencement of its development the yolk sac shows a certain amount of differentiation. Its epithelium forms glandlike invaginations (Graf Spee). According to Meyer and Jordan, epithelial buds, solid or hollow outgrowths—structures rather variable in appearance—occur at the end of the first month and project into the mesoderm. Later the epithelium becomes flat and finally degenerates, with the thickening of the contents of the vesicle. These findings might be interpreted as indicating an early digestive and absorptive functional capacity of the epithelium (possibly gastric cells) lining the duct. This interpretation would also account for the disappearance of the early gastric cells lining the duct.

Greenblatt and his associates hold that none of these theories suffice exclusively to account for the findings. They regard the presence of heterotopic tissue in the omphalomesenteric duct as the result of retarded normal embryologic retrogression. They therefore present their theory on this basis in terms of "dysembryoma" which, as defined by Pierre Masson, is an example of vestigial heterotopia capable of becoming neoplastic (not a neoplasm).

An explanation of the presence of heterotopic tissue in Meckel's diverticulum, other than those previously advanced, seems to me to be suggested. Charles Davenport, discussing embryologic pathology before the Harvey Society two years ago, attempted to demonstrate that differences exist not only in the nuclei of the eggs of different species but also in those of the same species. If one could correlate standard nuclear variations in the egg with standard congenital malformations in the new-born, a definite pattern of malformation would be obtained.

On the basis of Davenport's theory, there is the possibility that the pattern of the nuclear particles may be disturbed so that the primordium of one organ is in part included in that of another. It is apparent, therefore, that if there is close contact of nuclear particles, giving rise to gastric mucosa and to mucosa of the small intestine, such tissues may become intermixed in fetal organs. This seems plausible when it is recalled that the stomach arises from the terminal portion of the foregut and the small intestine with its Meckel's diverticulum arises from the adjacent midgut. Incidentally, this might also explain why gastric mucosa is never found, for example, in the rectum, which arises from the relatively distant hindgut.

PATHOLOGIC STRUCTURE

The pathologic structure of Meckel's diverticulum is dependent to some extent on certain anatomic and embryologic factors.

The size of the opening of the diverticulum into the ileum is an important consideration. When it has a wide opening it permits

unhindered entrance and exit of intestinal contents. On the other hand, this wide lumen at its base undoubtedly accounts for the lodgment of a large variety of foreign bodies which have been discovered at operation, prominent among which are pins, seeds, bones, gallstones and intestinal parasites; even a Murphy button previously employed in a patient's gastro-enterostomy was found in his diverticulum three years later.[9] When the opening is narrowed, however, or restricted by a valvelike projection of redundant mucosa—which usually corresponds to an incomplete physiologic atresia—it may cause retention of intestinal contents, fecal stasis or impaction and result in dilatation of the distal end, with inflammation, perforation or intestinal obstruction.

The size of the diverticulum itself may reach such proportions as to produce actual torsion or volvulus of the bowel. This is likely to occur in larger types of diverticula with constricted bases. Mathews [3] reported a diverticulum the size of a hen's egg with a narrow pedicle, causing strangulation of 20 inches (50 cm.) of small intestine by volvulus. In case 21 (fig. 5) of the present series, to be referred to later, a rather large pendulous diverticulum caused partial obstruction by torsion of the segment of ileum to which it was attached.

A diverticulum may occasionally form part of the contents of a hernia (most frequently either inguinal or femoral) and has even been known [3] to have been brought down into the scrotum by descent of the testis to which it was adherent. Another unusual case is that of Brodnax [10] in which a sciatic hernia contained an adherent Meckel's diverticulum, measuring 4 inches (10 cm.) in length. On the whole, however, these cases are unusual. In Wellington's collected series [11] of 326 cases of Meckel's diverticulum (published in 1913), he found only 27 cases which belonged in this category.

The diverticulum may remain adherent to the umbilicus.[12] It is far more dangerous when the part adherent has been reduced to a cord of connective tissue, which, although quite slender, is usually firm and long and a potential source of interference with the intestinal function, either by angulation or torsion of the segment of the bowel or by constriction, causing ileus, intestinal infarction or obstruction. A case of this type was reported by Wellington [11] in which a loop of bowel about 1 foot

9. Peck, Charles H.: Murphy Button Retained for Three Years in Meckel's Diverticulum: Resection of Ileum; End-to-End Suture, Ann. Surg. **49**:134, 1909.

10. Brodnax, John W.: Sciatic Hernia: Report of a Case of Hernia of Meckel's Diverticulum Through the Greater Sciatic Foramen, J. A. M. A. **82**: 440-442 (Feb. 9) 1924.

11. Wellington, J. R.: Meckel's Diverticulum with Report of Four Cases, Surg., Gynec. & Obst. **16**:74-78, 1913.

12. Cullen, Thomas Stephen: Embryology, Anatomy and Diseases of the Umbilicus, Together with Diseases of the Urachus, Philadelphia, W. B. Saunders Company, 1916.

long, distended and deeply injected, was constricted by a diverticulum, from the tip of which was found a cord running to the umbilicus.

The fibrous strand may free itself from its umbilical anchorage and become adherent anywhere in the abdominal cavity—to the abdominal wall, to other portions of the intestine or to the omentum—and produce dangerous potentiality for the formation of loops, with resultant intestinal incarceration. This mechanism occurred in case 1 of the series presented herewith. And even without a fibrous band, the tip of the diverticulum when inflamed may attach itself to adjacent intestine and by its adherence cause partial or complete intestinal obstruction (at times with gangrene) by compression or constriction of an intervening loop of intestine. This happened in case 23.

Obstruction may also be caused by invagination of a diverticulum and thus lead to secondary intussusception. The relative frequency with which this is found is indicated in the reports of 160 cases collected from the literature by Harkins.[13] This condition is likely to occur when an unattached diverticulum becomes inverted, acting as a polyp in the lumen of the bowel.[14]

Meckel's diverticulum may be the site of a purely inflammatory process—so-called diverticulitis. It is acute inflammation of the diverticulum that offers the greatest difficulty from the standpoint of diagnosis. Here the types of inflammatory disease differ in no way from those of the appendix. One sees acute catarrhal inflammation as well as the graver, more dangerous, phlegmonous and gangrenous forms. Here, too, they may be complicated by perforation and abscess formation or by peritonitis. As in appendicitis, the tributaries of the portal vein may be involved in the purulent process of pylephlebitis and carry infective material to the liver, leading to the production of hepatic abscess.

As previously stated, Meckel's diverticulum frequently contains heterotopic tissue. Such a diverticulum is designated as "peptic." Gastric mucosa and pancreatic tissue are most generally found, in either case giving rise to ulceration and intestinal bleeding. These ulcers do not differ essentially from ulcers elsewhere, but the probability of their occurrence here is greater than in the stomach. In a diverticulum there are none of the normal physiologic inhibitory factors present in the normal stomach that militate against the production of peptic ulcer. In addition, a diverticulum and the adjacent small intestine are especially prone to spasm.[15] This definitely weakens the already poor defense

13. Harkins, Henry: Intussusception Due to Invaginated Meckel's Diverticulum: Report of Two Cases with a Study of One Hundred and Sixty Cases Collected from the Literature, Ann. Surg. **98**:1070-1095, 1933.

14. Wellington.[11] Mathews.[8]

15. Burger, W.: Ueber das Meckel'sche Divertikel mit Magenschleimhaut, Inaug. Dissert., Heidelberg, J. Hörning, 1932.

mechanism against the corrosive action of the gastric juice. These ulcers may go on to perforation, with subsequent peritonitis. Johnston and Renner,[16] who recently made a study of 62 previously recorded cases of definite ulcer formation in Meckel's diverticulum, reported perforation in 37 cases (59 per cent).

Neoplastic growths are found occasionally in Meckel's diverticulum. They may be either benign or malignant. According to Liccione,[17] on the basis of an extensive review of the malignant type, reports of only 12 undisputed cases had previously been published. To these he added a case of his own—one of spindle cell sarcoma—making a total of 7 cases of sarcoma, 4 of carcinoid disease and 2 of medullary carcinoma. In addition, there were recorded 3 cases of myxoma of indefinite origin and 3 cases of myxoma of dubious origin.

A granulomatous focus at the umbilicus may be the outward manifestation of an underlying patent or only partially obliterated omphalomesenteric duct. Wellington's study (1913) of 326 collected cases revealed 21 instances of umbilical fistula. These varied from minute openings with slight mucous discharge to those in which the whole intestinal contents were emptied through the umbilicus. Prolapse of the intestine may occur in these cases. Umbilical adenoma has also been found associated with an omphalomesenteric duct.[18]

Less frequently Meckel's diverticulum may be the site of tuberculous or typhoid ulceration and perforation. In the former it is likely to be associated with a similar condition in the intestine. Coley[19] reported an unusual case—the first to be published up to that time (1925)—in which the appendix was simultaneously involved in the tuberculous process. In typhoid, the ulceration or perforation is due to the presence of Peyer's patches in the diverticulum.

SYMPTOMATOLOGY

The symptomatology of Meckel's diverticulum is remarkably variable. In a large percentage of cases the anomaly does not give rise to any clinical symptoms whatsoever and is encountered incidentally at operation or at necropsy. On the other hand, when symptoms occur

16. Johnston, Lloyd B., and Renner, George, Jr.: Peptic Ulcer of Meckel's Diverticulum, Surg., Gynec. & Obst. **59**:198-209, 1934.

17. Liccione, W. T.: Malignant Tumor of Meckel's Diverticulum, Am. J. Surg. **34**:101-103, 1936.

18. (*a*) Koch, W., in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 4, pt. 1, pp. 175-182. (*b*) Faust, Louis S., and Walters, Waltman: Fibrosarcoma of a Meckel's Diverticulum Producing Intestinal Hemorrhage, Minnesota Med. **14**: 233-236, 1931.

19. Coley, B. L.: Tuberculosis of Meckel's Diverticulum Associated with Tuberculous Appendix, Arch. Surg. **11**:519-528 (Oct.) 1925.

from an underlying diverticulum, they are likely to simulate those of other acute abdominal conditions so closely that they may tax the diagnostic acumen of the most astute. The fact should be kept in mind, therefore, that Meckel's diverticulum is frequently associated with acute abdominal conditions and their complications.

Pain, when present, may be colicky and intermittent and is generally para-umbilical, as a rule to the right of the umbilicus; it may also manifest itself in the right iliac fossa. Nausea, vomiting and constipation may or may not occur. Anorexia is more frequently observed. In many instances blood is found in the stools, this at times being the only outstanding finding. The blood is usually dark but may be bright red and profuse. Fever, at least in the earlier stages, is rarely present. In the majority of cases, the symptoms as well as the pathologic changes resemble those seen in the various stages of appendicitis, for which condition involvement of Meckel's diverticulum is most generally mistaken, as reports in the literature amply testify. In cases of acute involvement, perforation, abscess formation or peritonitis may occur as a complication.

Obstruction caused by Meckel's diverticulum does not differ essentially from intestinal obstruction or intussusception due to other causes. According to estimates by Halstead,[20] on the basis of findings reported by Lichterstern as well as by Haven, Duchanssoy and by Brinton, Meckel's diverticulum actually is responsible for intestinal obstruction in 6 per cent of the cases. Harkins,[18] in his extensive and thorough study of collected cases, found that 17 per cent of the diverticula that cause trouble do so by producing intussusception.

Meckel's diverticulum with heterotopic tissue produces a clinical picture strikingly similar to the symptom complex of gastro-duodenal ulceration, with its attending complications. Cyclic pain is characteristic; it occurs not only with a periodicity in relation to the ingestion of food but also as "hunger pain," the secretion in the gastric mucosa here paralleling that in the duodenum. Perhaps the most outstanding diagnostic critera are melena and intestinal hemorrhage.

DIAGNOSIS

The diversity of pathologic lesions which may be induced by Meckel's diverticulum undoubtedly makes a positive diagnosis particularly difficult. Nor does the close simulation of its many lesions to other morbid conditions help in elucidating the problem. Nevertheless, one can hardly fail to be impressed with the gradual change of attitude which has been expressed in the literature during the past two decades, indicating an

20. Halstead, Albert Edward: Intestinal Obstruction from Meckel's Diverticulum, Ann. Surg. **35**:471-494, 1902.

approach to more positive diagnosis, especially in those cases in which bleeding occurs, even though the diagnosis may be established by exclusion.

Tarry stools or intestinal hemorrhage should no longer fail to arouse a suspicion of Meckel's diverticulum. Farr and Penke [7] recently reported 4 cases, in all of which the diagnosis was made prior to operation. Persistent bleeding from the diverticulum occurred in all of these instances; in 2, bleeding may have been due to intussusception. The occurrence of bloody stools may also point to the development or the presence of a heterotopic peptic ulcer, and in the adult it may not give rise to any other symptoms. This type of ulcer may closely simulate gastric or duodenal ulcer, from which it may be differentiated roentgenographically. Intestinal hemorrhage and secondary anemia (as in the case of fibrosarcoma reported by Faust and Walters [18b]) may be the only apparent symptoms, even in the presence of a malignant condition. Intestinal bleeding in young children should be differentiated from hemophilia (in which there is a positive family history), purpura hemorrhagica (with the presence of petechiae) and hemorrhagic disease of the new-born.

Intussusception in children under 2 years of age is rarely caused by Meckel's diverticulum. In older children or adults intussusception due to Meckel's diverticulum should suggest itself as a possibility.

It is the inflammatory manifestations of Meckel's diverticulum that are most difficult to diagnose preoperatively. Therefore, at operation, in the absence of an adequate pathologic condition to explain the clinical findings, Meckel's diverticulum should be sought.

Clinically, abdominal pain, vomiting and intestinal bleeding represent the most significant diagnostic criteria of Meckel's diverticulum. From the roentgenologist's point of view, however, a roentgenogram may offer additional diagnostic evidence. Meckel's diverticulum may be pictured in serial roentgenograms of the gastro-intestinal tract. Routine methods, however, may reveal nothing more than a suggestion of the necessity for further detailed examination. An informed roentgenologist directs his attention specifically to study of the small intestine, since the problem requires a different technic and contrast mixture than those employed in routine studies of the esophagus, stomach and colon. A larger quantity of barium sulfate and water, with more frequent observations during the passage of the meal, are requisite. Greater diagnostic accuracy in lesions of the small intestine is possible by this method.

PROGNOSIS AND MORTALITY

The prognosis following operation for Meckel's diverticulum, by and large, is favorable. Mathews [8] reported 3 fatalities in his series of 9 cases in which clinical symptoms were evident. Wellington,[11] in his

study of 326 collected cases, found a higher mortality (40 per cent), and added a note to the effect that the high death rate compared to that for appendicitis is probably due to the greater liability to early perforation with less tendency to localization of the infection, the frequent involvement of the bowel and the greater mechanical difficulty in removal.

Two of the 23 cases in the series reported here terminated fatally. In 1 death was due to a complicating bronchopneumonia and in the other to postoperative ileus.

REPORT OF CASES [21]

CASE 1.—A boy 6 months of age had colicky abdominal pains at irregular intervals for several weeks prior to admission to the hospital. Tarry stools were followed by dark red and, finally, bright red intestinal bleeding. There was a palpable mass in the right lower quadrant. Meckel's diverticulum was found at operation in the lateral wall of the ileum, 12 inches from the ileocecal junction; a small fibrous band from the diverticulum was adherent to the adjacent small intestine, compressing and obstructing the intervening 2 feet (60 cm.) of intestine. Pathologic examination of the diverticulum showed accessory pancreatic tissue with chronic interstitial pancreatitis in the submucosa at the tip of the diverticulum, adjacent to a chronic ulcer, approximately 3 mm. in diameter. The surface of the ulcer was covered by fibrinous exudate and showed polymorphonuclear and lymphocytic infiltration down to the muscular coat (fig. 1). There was no intestinal bleeding subsequent to diverticulectomy.

CASE 2.—A man aged 31 had epigastric abdominal pain and nausea and had been vomiting for two days. There were rigidity and tenderness in the right lower abdominal quadrant. The white cell count was 11,000, with 90 per cent polymorphonuclears. Operation disclosed a gangrenous appendix and Meckel's diverticulum, approximately 2 inches (5 cm.) long and edematous at the tip. Pathologic examination of diverticulum showed it to be thin walled (2 mm.) with congested serosa.

CASE 3.—A boy 7 months of age was acutely ill and had a tense distended abdomen. The white cell count was 15,600, with 87 per cent polymorphonuclears. A diagnosis of perforation of the appendix was made. A perforated diverticulum with an abscess was found on operation. Pathologic examination (at necropsy) showed chronic adhesive peritonitis involving the lower portion of the ileum and the anterior peritoneum and diffuse bronchopneumonia.

CASE 4.—A man aged 62 had intermittent "crampy" epigastric abdominal pain with seasonal (winter) periodicity for thirteen years. Examination elicited epigastric tenderness. The white cell count was 6,100 with 53 per cent polymorphonuclears. Operation disclosed cholecystitis with lithiasis and a diverticulum 2 inches long, with a large opening at the base into the ileum. Pathologic examination of the diverticulum did not reveal anything remarkable.

CASE 5.—A man aged 26 had abdominal pain and nausea and had vomited repeatedly for two days. Appendectomy had been performed nine months previously for acute purulent appendicitis. The abdomen was distended and tender. The white cell count was 21,200, with 83 per cent polymorphonuclears. Operation disclosed a perforated gangrenous diverticulum 15 inches (38 cm.) from the ileo-

21. These reports were taken from the surgical files of the New York Post-Graduate Medical School and Hospital, Columbia University.

cecal junction, causing kinking and obstruction of the small intestine. Pathologic examination of the diverticulum showed it to be dark gray, hemorrhagic and necrotic, with a narrow pedicle, and covered by fibrinous exudate. The glandular stroma was infiltrated with lymphocytes, mononuclear cells and occasional polymorphonuclear leukocytes.

CASE 6.—A man aged 36 had severe abdominal pain and had been vomiting for four days. There was slight abdominal distention, with tenderness and rigidity

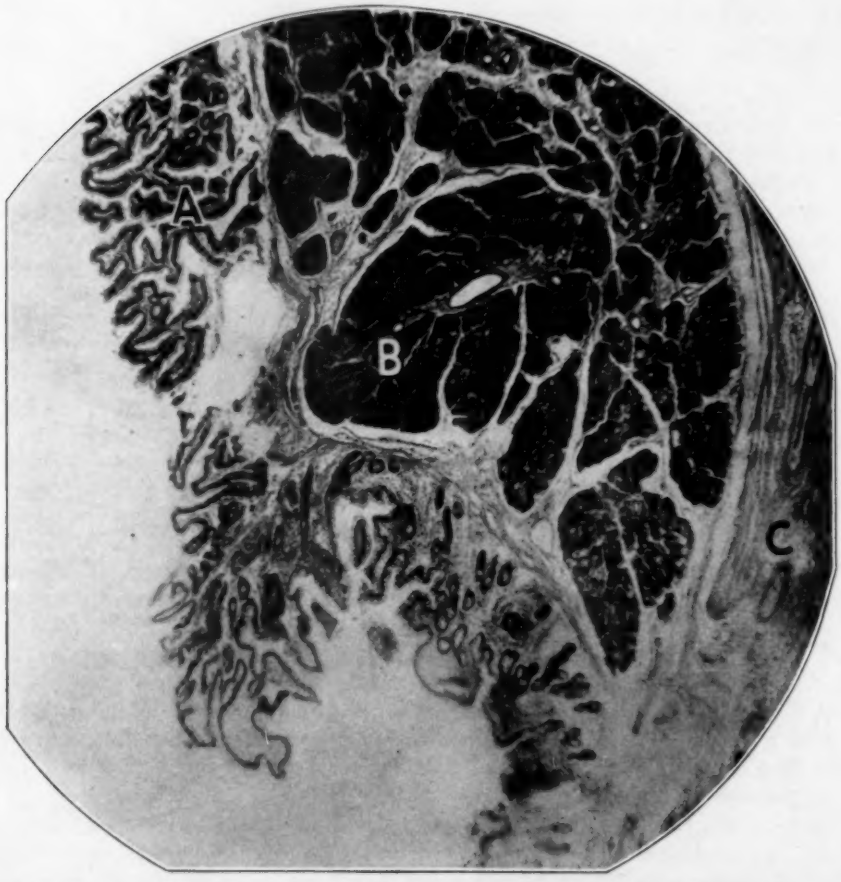

Fig. 1 (case 1).—Photomicrograph of the tip of Meckel's diverticulum. *A* indicates the mucosa, with somewhat tortuous glands; *B*, the accessory pancreatic tissue embedded in submucosa, and *C*, the muscle layer. Medium high power magnification.

in the right lower abdominal quadrant. The white cell count was 9,650, with 65 per cent polymorphonuclears. Operation disclosed a perforated gangrenous appendix, with an abscess, and a diverticulum, 4 inches (10 cm.) long and 15 inches (38 cm.) from the ileocecal junction which showed no pathologic changes. Surgeon's note: "The diverticulum ordinarily would have been removed, but in this case it was deemed unwise in the presence of such a fulminating infection."

CASE 7.—A woman aged 43 had generalized cramplike pains in the lower part of the abdomen of four days' duration. Her appetite was poor. There was tenderness in the lower abdominal quadrants, that on the left being most marked. The white cell count was 15,750, with 87 per cent polymorphonuclears. Operation showed subsiding acute appendicitis, multiple fibroid tumors, an ovarian cyst on the right side, hydrosalpinx on the left side, carcinoma of the cervix uteri and a diverticulum 1 inch (2.5 cm.) long, 2½ feet (75 cm.) from the ileocecal junction. Pathologic examination of the diverticulum did not reveal anything remarkable.

CASE 8.—A woman aged 40 had recurrent "nagging pain" in the right lower abdominal quadrant and slight nausea of two years' duration. Examination showed tenderness in this quadrant. Operation disclosed subacute cholecystitis, obliterative appendicitis and a diverticulum—a small "nipple-like" protrusion 16 inches (40 cm.) from the ileocecal junction. Pathologic examination of the diverticulum did not reveal anything remarkable.

CASE 9.—A woman aged 35 had cramplike abdominal pain preceded by diarrhea. There was tenderness in the right lower abdominal quadrant. Operation disclosed obliterative appendicitis and a diverticulum approximately 2 inches long and 4

Fig. 2 (case 9).—Meckel's diverticulum showing the narrow pedicle and the dilated diverticulum both lined with intestinal mucosa in typical folds.

inches from the ileocecal junction. Pathologic examination of the diverticulum showed a smooth outer surface and injected blood vessels containing an excess number of polymorphonuclear leukocytes (fig. 2).

CASE 10.—A boy aged 10 years had severe abdominal pains recurring from three to four times a week over a period of one year. There were frequent nausea, vomiting occurring only once with an attack of pain, generalized abdominal distention, slight tenderness in the right lower quadrant and spasm of the rectus muscle. The white cell count was 8,600 with 47 per cent polymorphonuclears. Operation disclosed subacute appendicitis and a diverticulum with a complete mesentery, 20 inches from the ileocecal junction. Pathologic examination of the diverticulum showed sudden narrowing in the diameter from 13 mm. at the base to 8 mm. in the distal portion, marked congestion of the serosal vessels and excess polymorphonuclear leukocytes in some of the blood vessels (figs. 3 and 4).

CASE 11.—A man aged 25 had recurrent attacks of generalized abdominal pain, lasting from one to two hours and localized in the right lower abdominal quadrant, over a period of one year, and suffered from belching after meals. There was slight tenderness in the right lower abdominal quadrant. The white cell count was 10,400, with 69 per cent polymorphonuclears. Operation disclosed subsiding acute

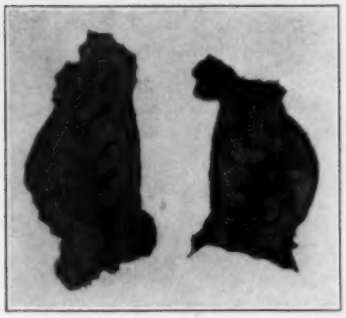

Fig. 3 (case 10).—Meckel's diverticulum with a lining of intestinal mucosa. The lumen shows a bifurcation at the tip.

Fig. 4 (case 10).—Photomicrograph of the tip of the specimen shown in figure 3. *A* indicates the mucosa with well formed glands; *B*, the lymph follicle, and *C*, the muscle layers, both circular and longitudinal. Medium high power magnification.

appendicitis and a diverticulum 3 inches (7 cm.) long, 3 feet (90 cm.) from the ileocecal junction. Pathologic examination of the diverticulum showed chronic inflammation with extravasation of blood beneath the mucosa.

CASE 12.—A man aged 22 had "crampy" pain in the lower abdominal quadrant almost daily for three weeks. There were slight spasm and tenderness in the right lower quadrant. Operation showed subacute appendicitis and a diverticulum approximately 2 inches long, 20 inches from the ileocecal junction. The diverticulum was bifurcated at the tip. Pathologic examination showed intense infiltration with eosinophilic leukocytes and slight edema of the subserosal connective tissue.

CASE 13.—A woman aged 52 had recurrent pain in the region of the gallbladder, gaseous eructations and indigestion after meals of twelve years' duration. There was a history of jaundice. Deep tenderness was elicited in the right lower abdominal quadrant. Operation revealed chronic appendicitis and cholecystitis and a diverticulum 1 inch in length. Pathologic examination of the diverticulum showed several small pouchlike extensions at the tip and thickening of the adventitia of the vessels in the submucosa. (Fatal termination was due to subsequent postoperative ileus.)

CASE 14.—A woman aged 28 for fourteen years had severe attacks of pain in the right lower abdominal quadrant, with slight nausea and anorexia during the attacks. There was slight tenderness on palpation. Operation disclosed chronic appendicitis and a diverticulum 2 inches long. Pathologic examination of the diverticulum did not reveal anything remarkable.

CASE 15.—A boy aged 5 years suffered from acute abdominal pain and nausea of twenty-eight hours' duration. The pain occurred first in the epigastric region and later in the right lower quadrant. The white cell count was 15,400, with 79 per cent polymorphonuclears. There were rigidity and tenderness in the right lower quadrant. Operation disclosed acute appendicitis and a diverticulum 2 inches long with its own mesentery, 20 inches from the ileocecal junction. Pathologic examination of the diverticulum did not reveal anything remarkable.

CASE 16.—A boy aged 7 years had pain in the right lower abdominal quadrant of three days' duration; a similar attack of one day's duration occurred fifteen days previously. There was slight generalized abdominal tenderness. The white cell count was 7,450, with 68 per cent polymorphonuclears. Operation disclosed chronic appendicitis and a small diverticulum. Pathologic examination of the diverticulum did not reveal anything remarkable.

CASE 17.—A man aged 46 had a dull aching pain in the right side of the abdomen and nausea of seven months' duration and extreme pallor, with loss of weight and weakness, of over three months' duration. Examination revealed tenderness on the right side of the abdomen, with the suggestion of a palpable mass. The white cell count was 13,600, with 86 per cent polymorphonuclears. Operation disclosed a carcinoma of the cecum and the ascending colon and a diverticulum approximately 1 inch long at the terminal portion of the ileum. Pathologic examination of the diverticulum did not reveal anything remarkable.

CASE 18.—A man aged 32 suffered from abdominal pain, nausea and vomiting of sixteen hours' duration. He gave a history of recurrent attacks of cramps once a year. Exploratory laparotomy with drainage had been performed for a perforated appendix with peritonitis six years previously. (The appendix was not removed.) There was moderate distention of the abdomen, with tenderness in the right lower quadrant. The white cell count was 11,200 with 81 per cent polymorphonuclears. Operation disclosed acute appendicitis and a diverticulum 3 inches

long and the diameter of the thumb. Pathologic examination of the diverticulum showed marked congestion and edema of the submucosa with an abundance of dilated blood vessels.

CASE 19.—A girl aged 15 years had cramps in the right lower abdominal quadrant and pain in the upper quadrant with nausea, vomiting and anorexia of two days' duration. There were spasm and tenderness in the right lower quadrant. The white cell count was 11,500, with 74 per cent polymorphonuclears. Operation revealed acute appendicitis, a Lane's kink and a diverticulum 3 inches (7 cm.) long with a small mesentery at the base, 18 inches (45 cm.) from the ileocecal junction. Pathologic examination of the diverticulum did not disclose anything remarkable.

CASE 20.—A woman aged 23 had attacks of pain in the right lower abdominal quadrant with nausea and constipation of two years' duration. There was tenderness in the right lower quadrant. Operation disclosed chronic appendicitis and a diverticulum at the mesenteric border of the ileum, 3 feet (90 cm.) from the ileocecal junction. Pathologic examination of the diverticulum did not reveal anything remarkable.

CASE 21.—A woman aged 62 had pain in the epigastric region and the right lower abdominal quadrant of sudden onset, with nausea and diarrhea lasting for two days. There were abdominal rigidity and tenderness in the lower quadrants, most marked to the left and just below the umbilicus. The white cell count was 8,700, with 56 per cent polymorphonuclears. Operation disclosed a small fibrotic appendix which was not considered an adequate cause of the symptoms. Exploration revealed a large pendulous diverticulum, 20 inches from the ileocecal junction and filled with approximately 3 ounces (90 cc.) of serous fluid. The diverticulum had rotated and caused torsion and partial obstruction of a segment of the ileum to which it was attached by a broad base. Pathologic examination of the diverticulum revealed a low grade chronic inflammation, with a moderate number of lymphocytes and plasma cells in the subserosa and muscularis (fig. 5).

CASE 22.—A woman aged 66 had prolapse of the uterus and goiter of fifteen years' duration. Operation disclosed an atrophic uterus and adnexa, an obliterated appendix and a diverticulum. Pathologic examination of the diverticulum did not disclose anything remarkable except for sacculations of the cavity.

CASE 23.—A girl aged 7½ years had repeated attacks of cramplike abdomnial pains with vomiting and absence of defecation. The attacks were of three days' duration. Appendectomy had been performed four months previously. Generalized abdominal rigidity and tenderness were present, being more marked just above the umbilicus. The white cell count was 7,600, with 46 per cent polymorphonuclears and 50 per cent lymphocytes. Operation disclosed a diverticulum 22 inches (55 cm.) from the ileocecal junction with the tip of the diverticulum adherent to the cecum at the site of the recent appendectomy; traction by the diverticulum was causing angulation and obstruction of the ileum and gangrene of the intervening segment of the bowel.

ANALYSIS OF CASES

This series, a total of 23 cases, represents instances of Meckel's diverticulum found in the course of laparotomies done in the surgical division of the New York Post-Graduate Medical School and Hospital (abdominal operations in other departments not included), as revealed

by a search of the surgical files for a period of seven years (1930-1936 inclusive). The distribution according to years was as follows: 2 in 1930, 2 in 1932, 4 in 1933, 10 in 1935 and 5 in 1936, with an average incidence of 0.24 per cent.[22] These reports by no means represent all

Fig. 5 (case 21).—*A*, Meckel's diverticulum showing sacculations on the serosal surface. *B*, The same specimen. A cavity with prominent mucosal folds and secondary diverticula are seen.

22. The average incidence of 0.24 per cent for the entire period was computed on the basis of these percentages: 0.15 per cent for 1930 and 1932; 0.3 per cent for 1933; 0.73 per cent for 1935, and 0.36 per cent for 1936. The total number of laparotomies performed was 9,557, and the yearly average was 1,365 laparotomies.

cases on record at the hospital. Prior to 1930 there were, among others, several instances of intussusception and perforation by a foreign body.[23]

It is interesting to note that although the incidence of males to females is reported in the literature as 4:1, 3:1 and 2:1, and in 1 instance [6] as 2:3, the proportion in the present series is 13:10. The age distribution ranges between 6 months and 66 years.

For the purpose of analysis, the cases in this series have been divided into groups based on surgical and pathologic data (see table), patterned after a workable classification given by Greenblatt, Pund and Chaney.

Diverticulitis Group.—In case 3, in which there were perforation of the diverticulum and abscess, autopsy showed chronic adhesive perito-

Analysis of Data

Group of Cases	Number of Cases	Findings	Symptomatology
(*a*) Diverticulitis group	10 (2 in *b*)	Acute with gangrene and perforation (cases 3 and 5); acute congestion (cases 2, 9, 10, 12 and 18); chronic inflammation (cases 11, 13 and 21); foreign bodies	Essentially that of appendicitis
(*b*) Obstructive group	4 (2 in *a*) (1 in *d*)	Volvulus (case 21); bands and adhesions (cases 1, 5 and 23); intussusception; contents of hernia	Essentially that of intestinal obstruction
(*c*) Incidental group	11	Not remarkable pathologically (cases 4, 6, 7, 8, 14, 15, 16, 17, 19, 20 and 22)	Not pronounced
(*d*) Heterotopic (peptic) group	1 (also in *b*)	Pancreatic tissue (case 1); gastric mucosa with or without ulceration, hemorrhage, perforation and peritonitis	Mimicry of gastroduodenal ulcer; tarry or bloody stools; perforation
(*e*) Neoplastic (tumor) group	0	Benign: enterocystoma, adenoma, fibroma, myoma and carcinoid; malignant: carcinoma and sarcoma	Intestinal bleeding; intussusception; obstruction
(*f*) Umbilical group	0	Adenoma or granulomatous focus; umbilical or fecal fistulas	Referable to umbilicus

nitis involving the lower end of the ileum and the anterior abdominal wall and diffuse bronchopneumonia.

In case 5 gangrene and perforation of the diverticulum caused kinking and obstruction of the small intestine by fibrinoplastic adhesions.

In the remainder of the cases in this group either acute congestion or chronic inflammation of the diverticulum was found.

Obstructive Group.—In case 21 a rather large, pendulous and fluid-filled diverticular sac had rotated and caused partial obstruction by torsion of the segment of the ileum from which it arose (fig. 5).

23. An additional case has been encountered at the hospital since the reading of this paper at the New York Academy of Medicine. The patient, who had undergone an appendectomy several years previously, was admitted for the repair of a ventral hernia. During the course of an exploratory examination a diverticulum was found which (as in case 1 of the series herewith presented) contained pancreatic tissue.

In case 1 a small fibrous band from the tip of the diverticulum was adherent to the adjacent intestine and caused obstruction by compressing an intervening loop of intestine, while in case 23 adherence of the tip of the diverticulum to the cecum (site of a recent appendectomy) caused angulation, obstruction and gangrene of the intervening segment of bowel.

Case 5 has been referred to under the preceding group.

Incidental Group.—None of the diverticula in this group of cases showed anything remarkable, either clinically or pathologically.

Heterotopic Group.—Histologically, the diverticulum in case 1 showed the presence of accessory pancreatic tissue in the submucosa at the tip (fig. 1). Adjacent to the pancreatic tissue, showing chronic interstitial pancreatitis, was a definite chronic ulcer approximately 3 mm. in diameter, with its surface covered by fibrinous exudate and with polymorphonuclear and lymphocytic infiltration down to the muscular coat. The manner in which obstruction was caused by the fibrous band of this diverticulum is referred to previously (obstructive group). With the exception of this case, the diverticula in this entire group of cases were lined throughout by small intestinal mucosa.

Neoplastic (Tumor) Group and Umbilical Group.—There were no cases representing either of these groups.

COMMENT

An analysis of reported cases indicates that many instances of persistent postoperative syndrome, particularly after operations on the right lower abdominal quadrant, are due to the undiscovered presence of Meckel's diverticulum. This is borne out by the frequency with which a diverticulum has been revealed as the site of the pathologic process. The fact that a gradually increasing number of Meckel's diverticula are found by reason of specific search in the course of abdominal operations would seem further to indicate the advisability of suspecting the presence of Meckel's diverticulum in puzzling abdominal conditions.

It should perhaps be emphasized that because of the possibility of postoperative obstruction, initiated by edema or by the inverted stump, special caution should be exercised in the technic in dealing with the base of the diverticulum to avoid diminishing the caliber of the intestinal lumen. In rare instances, when a short diverticulum was inverted instead of being removed it has been known to cause intussusception of the bowel.

The opinion has been repeatedly expressed that whether diseased or not Meckel's diverticulum should be removed, since its existence is considered a greater menace than an appendix, owing to the serious lesions to which it may give rise. As a corollary to this, defense is offered for

the paramedian (rectus) incision, through which more adequate exploration can be made, in preference to the McBurney incision, even though the surgical indication appears to be merely for appendectomy.

Unfortunately it is difficult to obtain adequate data about the more common disturbances of Meckel's diverticulum. In studying the literature one is impressed particularly with the fact that the majority of references are concerned with case reports made interesting by some bizarre type of pathologic process.

The many types of lesions with which Meckel's diverticulum is involved make it one of the gravest mimics of other abdominal conditions. Its significance in routine abdominal operations is therefore quite apparent, and it seems to merit more attention as a purely surgical problem than it has been given.

SUMMARY

The embryology and anatomy of Meckel's diverticulum are briefly reviewed.

Heterotopic tissue in Meckel's diverticulum and the various theories of its origin are discussed.

An analysis of a series of 23 case histories is presented on the basis of the pathologic process present and the mechanisms giving rise to abdominal crisis.

The symptomatology and significance of Meckel's diverticulum in routine abdominal operations are stressed, and special emphasis is given to its mimicry of acute abdominal conditions.

Diagnostic criteria of lesions of Meckel's diverticulum are evaluated.

Prognosis and mortality rate are included.

125 East Sixty-Third Street.

OX FASCIA LATA FOR RECONSTRUCTION OF ROUND LIGAMENTS IN CORRECTING PROLAPSE OF THE VAGINA

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For many years grafts of fascia lata, either autogenous or heterogenous, have been used for the repair of hernia. Autogenous and heterogenous grafts of tendons have also been used to replace tendons lost by injury or disease. The history of the use of these grafts has been so aptly reviewed recently that it little behooves me to repeat it here. The reader is referred especially to an article by Koontz,[1] which outlines the history of the use of fascia for grafts and of the development of preserved fascia for grafts and sutures. To Koontz belongs the credit for devising a practical method of preserving the fascia lata of the ox so that it can be kept in the operating room for use at a moment's notice, as any other suture material. This saves the time of a second operation to obtain autogenous fascia. The success[2] of this preserved fascia for sutures led Koontz to use larger pieces to repair defects in hollow viscera.[3] It is the purpose of this paper to report another use for preserved fascia. Before making this report, I consulted Koontz and the literature and found no other reference to any form of fascia being used to reconstruct round ligaments or to suspend the vaginal vault after panhysterectomy.

My attention was first called to the need of some material to suspend the vagina from above about ten or twelve years ago, when associated

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Read before the Baltimore Obstetrical and Gynecological Society, Feb. 12, 1937.

1. Koontz, A. R.: Experimental Results in the Use of Dead Fascia Grafts for Hernia Repair, Ann. Surg. **83**:523-536 (April) 1936.

2. Koontz, A. R.: Healing in Hernia Repair, Internat. S. Digest **4**:195-198 (Oct.) 1927; Dead (Preserved) Fascia Grafts for Hernia Repair: Clinical Results, J. A. M. A. **89**:1230-1234 (Oct. 8) 1927; New Principles and Procedures in Hernia Repair, Texas State J. Med. **24**:259-265 (Aug.) 1928; Preserved Fascia in Hernia Repair, with Special Reference to Large Postoperative Hernia, Arch. Surg. **26**:500-509 (March) 1933; Suture Material for Hernia Repair, with Special Reference to Preserved Fascia Strips, South. M. J. **25**:372-380 (April) 1932.

3. Koontz, A. R.: Experimental Results in the Use of Dead Fascia Grafts for Repair of Defects in Hollow Viscera, South. M. J. **22**:417-422 (May) 1929.

with Howard A. Kelly. He had a patient with a large vesicovaginal fistula which followed irradiation of a carcinoma involving the entire trigonum, the destruction of the tumor obviously resulting in a large opening. The ureters emptied into each side of the fistula, and the bladder prolapsed through the opening into the vagina, presenting at the outlet. Various attempts to hold it up mechanically with pessaries or glass balls failed. Abdominal suspension of the bladder was likewise unsuccessful. I believe that fascia lata could be used to suspend such a bladder to the anterior abdominal wall, as I did in the case of prolapse of the vagina herein reported.

In January 1933, when confronted with a prolapse of the vagina three years after panhysterectomy, I hit upon the idea of suspending the vault with fascia lata. The following report includes a summary of the history and the operative notes:

Mrs. R. P., aged 57, was referred by the late Dr. Frederick Detrick because of vaginal bleeding of a few days' duration. Dilatation and curettage revealed early adenocarcinoma. On March 27, 1930, bilateral salpingo-oophorectomy, panhysterectomy and appendectomy were performed. After the uterus was removed "one cigaret drain was left in the vagina and the vaginal fornix was closed with chromic catgut sutures; stumps of the round ligaments and infundibulopelvic ligaments were sutured to the fornix of the vagina." The raw surface was covered over by suturing the peritoneum of the bladder "to the posterior vaginal wall." An uneventful recovery ensued, except for a slight low grade infection in the fat abdominal wall.

On July 8, 1931, the patient returned to the office, giving the following history: About five or six weeks before this visit, while spading in the garden, all of a sudden she felt "something give way" and "something came out of her body." Her general health had been good, and she had gained some weight since the operation. She was in excellent general condition, but there was marked prolapse of the vagina, particularly of the anterior wall, on straining, the vault coming down to the outlet (fig. 1). There was no evidence of recurrence of the carcinoma, either on abdominal or on pelvic bimanual palpation. A second degree perineal laceration had been present from childbirth twenty-five years or more before. Apparently two factors had contributed to this prolapse: first, a weakened perineal floor and, second, a severe strain, which tore the vagina away from the suspending round and broad ligaments. A Gehrung pessary inserted as a trial support was unsatisfactory. On one occasion the vagina actually prolapsed through the pessary after a long shopping tour.

The patient was not seen again until Jan. 17, 1933. During the interval there had been continual discomfort. The abdominal scar of the previous operation was well healed. There was definite tenderness about 3½ inches (8.9 cm.) to the left of the umbilicus, but no masses were made out. The family physician, however, had felt "something loose in the left flank," which he took to be a metastatic abdominal tumor. There was a little resistance over the left lower quadrant at the point of tenderness.

The vaginal outlet admitted two or three fingers; the external genitalia were otherwise normal. Straining brought both walls of the vagina, but especially the anterior wall, down through the outlet. The pelvis was otherwise normal.

A careful roentgenographic study was made for an intra-abdominal or gastro-intestinal tumor. None was found. A roentgenogram of the chest showed no evidence of metastasis.

The patient then entered the hospital for exploratory laparotomy and such suspension of the vaginal vault as would be possible. The operation was performed on January 26. After the abdomen and pelvis had been prepared in the usual manner, the low midline scar of the previous operation was excised down to the fat and the abdomen was opened. The omentum, which was densely adherent to the line of incision, required difficult dissection for its release. The viscera in the upper part of the abdomen were normal, and the pelvis contained some adhesions which were released fairly easily. The vaginal vault was low, extending only about halfway or less to the anterior abdominal wall; as a matter of fact, it did not

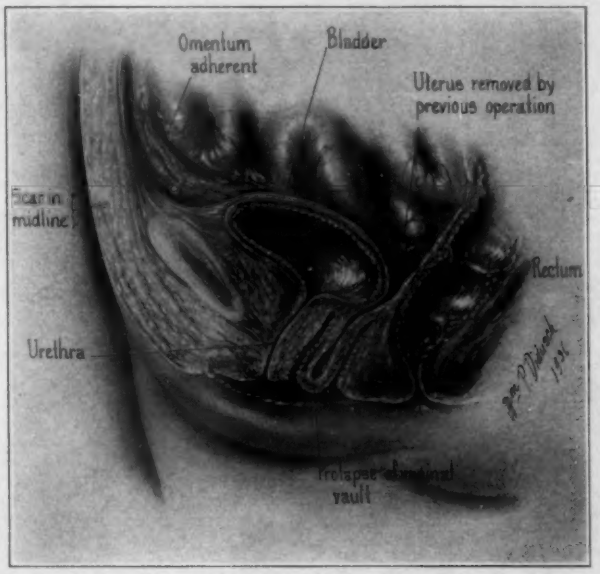

Fig. 1.—The condition of the patient at the time of operation.

extend as high as the vertex of the bladder. There were no enlarged glands and no evidence of recurrence of the original disease. The problem was simply one of suspension of the vaginal vault.

After several minutes of careful study, during which various plans were thought of and discarded, the following procedure, which proved to be most satisfactory, was decided on, that is, intra-abdominal suspension of the vaginal vault by round ligaments reconstructed from fascia lata. One strong suture of ox fascia lata, in a Koontz fascia needle, was placed through the vaginal vault on the right side, as illustrated in figure 2. The needle was then carefully worked laterally under the peritoneum to the lateral pelvic wall near the internal abdominal ring and continued forward to be anchored to the anterior surface of the posterior sheath of the rectus muscle. The other end of the suture, which was left long, was rethreaded into a similar needle and brought anteriorly under the peritoneum of the bladder to the symphysis, and through the sheath of the rectus muscle to be anchored to the anterior surface of the posterior sheath of the muscle 1 inch

(2.5 cm.) below the other end of this same suture. The ends of the suture were anchored in place with black silk. The suture supported the vaginal vault and bladder so securely that a similar suture was placed on the left side, the first part going out under the old broad ligament subperitoneally and around the pelvic wall and anterior abdominal wall to be anchored in the posterior sheath of the rectus muscle. The other end of the suture was brought forward like the one on the right, under the peritoneum of the bladder and through the abdominal wall, just above the symphysis. This gave excellent support to the vaginal vault, the weight of which was equally distributed through these new round ligaments.

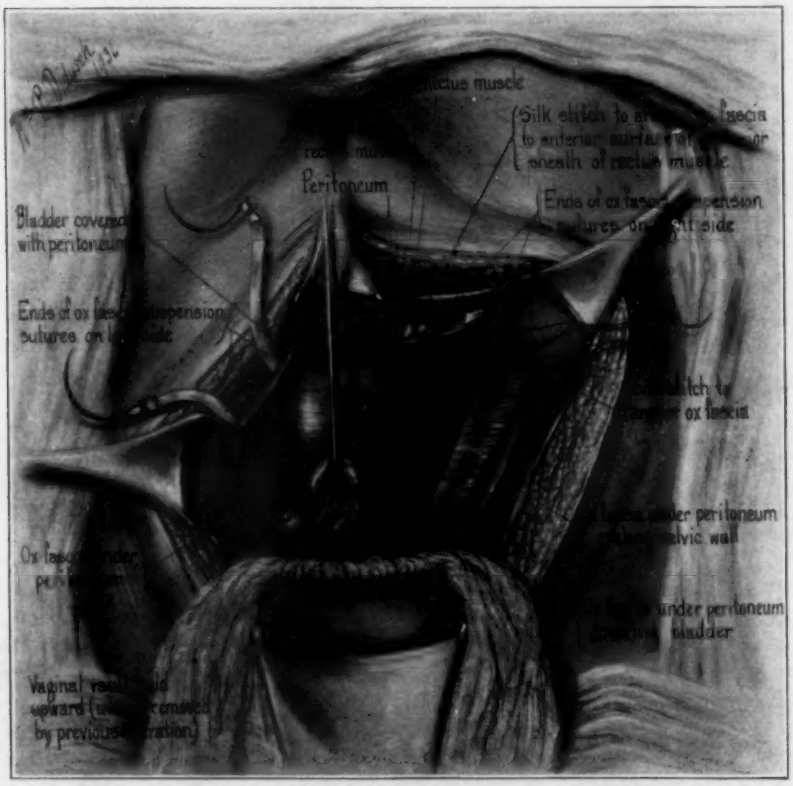
Peritoneum
Bladder covered with peritoneum
Ends of ox fascia suspension sutures on left side
Ox fascia under peritoneum
Vaginal vault drawn upward by previous suspension

Fig. 2.—The method of placing suspension sutures of ox fascia to draw and hold the vault of the vagina upward.

In placing these sutures, several fundamental principles had to be remembered: This transplanted tissue would not become an integral part of the host unless embedded in a vascular area to allow its reorganization. The fascia could not be left as "guy-ropes" across the peritoneum to catch and kink a loop of bowel. The suture had to be completely hidden. As the fascial suture was rather long, the unused end was worked under the peritoneum of the bladder to give added support to this organ, so that its weight, when full of urine, would not force down the vagina or bring undue strain on the newly made round ligaments. It would have been possible to have buried these sutures by splitting the peritoneum, laying in the

suture and resuturing the peritoneum, but this would have required more time. The shorter technic was to run the needle under the peritoneum for its full length, then bring it out and reinsert it in the same needle hole, continuing subperitoneally, step by step, until the fascial strip was brought to the desired point for anchor. There was practically no raw surface left at these points of exit and entrance through the peritoneum, and no secondary suture of the peritoneum had to be made over these.

The operation took about two hours, but under ordinary circumstances the time could be cut down materially. Several items added to the length of the opera-

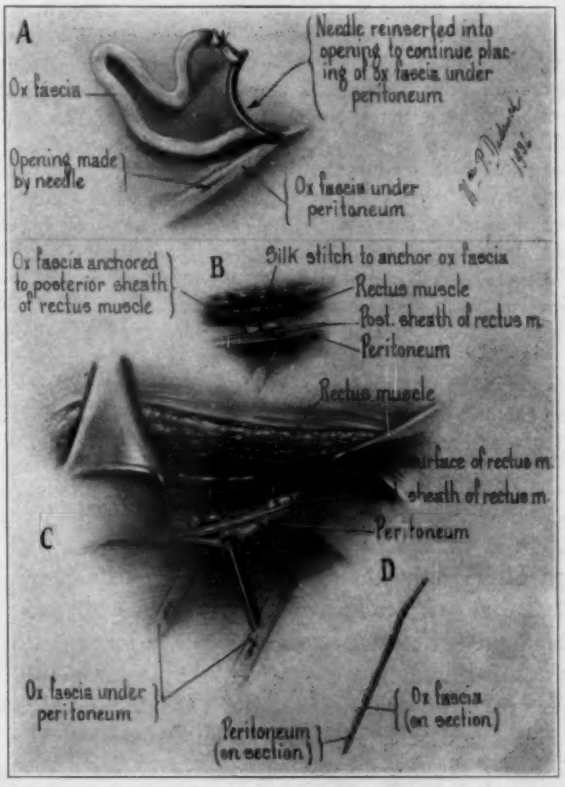

Fig. 3.—*A*, the method of placing the sutures under the peritoneum; *B*, the method of anchoring the sutures; *C*, the detail of anchoring the sutures to the sheath of the rectus muscle, and *D*, the relation of the fascial suture to the peritoneum—a sectional view.

tion: the dense omental adhesions, about one-half hour being necessary to get through them into the abdomen, and exploratory procedures about the abdomen and pelvis. The actual suspension of the vagina was carried out only after two or three other attempts proved of no value. In other cases, usually when the operation can be definitely planned in advance, no doubt the operative time could be reduced 50 per cent. Owing to this long procedure, it was deemed advisable not to

repair the perineum but to determine the necessity of such repair later. The abdominal incision was closed, and the patient left the operating room in good condition.

By February 3, eight days after operation, the patient had made a splendid recovery. All the stitches were out, and the wound had healed nicely. The anterior vaginal wall, which was suspended at operation, held in a perfectly straight line under the base of the bladder. A persisting rectocele was corrected on February 3 by posterior colporrhaphy, local anesthesia being used.

On February 9 the patient was discharged from the hospital to go home and rest in bed for a week or more. Examination on discharge showed that the wound of the second operation had healed nicely. The anterior vaginal wall still held firmly behind the bladder, forming practically a straight line from the urethral orifice to the vaginal vault.

At the last consultation on August 7 it was found that there had been no pelvic disorder, except a mild cystitis about three weeks before. One other attack had followed the first operation in March 1930.

Examination showed the abdomen to be normal. There was a well healed, low midline scar, which was slightly tender at the lower end, but there was no evidence of weakness. The perineum was well lifted and the scar well healed. When the patient strained there was little redundancy of the anterior vaginal wall. The vault was held up in good condition. With one finger in the vagina and the patient straining, no prolapse was noted. The outlet just admitted two fingers, with some discomfort to the patient. The upper portion of the pelvis was perfectly clear. Rectal examination gave negative results.

During the past four years, since the last examination, I have been in touch with the patient off and on and she still remains well. Her physician reported on Feb. 3, 1937, that she had no pelvic symptoms and no cystitis.

COMMENT

The problem at hand was the suspension of the vaginal vault which had prolapsed after panhysterectomy through a torn pelvic floor. This prolapse had carried with it the anterior vaginal wall and the posterior wall of the bladder. There was not, however, a large cystocele, indicating that some of the anterior portion of the urogenital diaphragm still held. There were two indications for abdominal section: first, the questionable metastatic nodule (which proved to be a phantom tumor) and, second, suspension of the vaginal vault. When the pelvis was exposed, no round ligaments were found to which to reanchor the vaginal vault. The vagina, which extended less than half way to the symphysis, was far too short to be fixed to the anterior abdominal wall according to the method of Brady [4] or of Thomas,[5] Kocher, Hempel,[6]

4. Brady, Leo: An Operation to Correct Genital Prolapse Following Vaginal Panhysterectomy, Am. J. Obst. & Gynec. **32**:295-299 (Aug.) 1936.

5. Thomas, T. Gaillard: Vulvar and Vaginal Enterocele, New York M. J. **42**:705-711 (Dec. 19) 1885.

6. Hempel, E.: Exohysteropexy (Kocher Method) for Prolapse in Elderly Women, Deutsche med. Wchnschr. **53**:1382 (Aug. 12) 1927.

Fraenkel [7] and Jarcho.[8] Nothing could be done with the vaginal vault through an abdominal incision unless the round ligaments were rebuilt out of preserved fascia lata. This was done as described.

Many methods of vaginal repair which do not require opening the abdomen have been advocated for decades. Some should be discussed here. Colpectomy or colpocleisis is serviceable only in noncohabitating women and would not have been suitable in my patient. Suspension of the vagina by opening it from below, according to the technic of Miller,[9] might have been adaptable, but there would have been great danger of injuring the adherent intestines in the pelvis, and such an injury could not have been discovered except by abdominal section. According to this method, the anterior vaginal wall is opened through an inverted T incision and the vaginal vault is anchored to the fascia in the region of the ureterosacral ligaments. The uteropubic fascia is then plicated under the bladder and the wound closed. This is followed by perineorrhaphy. Moschowitz [10] reported a technic by which the cul-de-sac of Douglas is obliterated with Pagenstecher or silk sutures through an abdominal incision. He and D. F. Jones [11] and others expressed the belief that a long cul-de-sac plays a prominent part in causing prolapsus uteri. In my case there was no pouch behind the vaginal vault to close.

With the method of Hundley [12] the uterus is delivered through an incision in the anterior vaginal wall and uterovesical peritoneum, as for an interposition operation. The redundant posterior vaginal vault is then brought out over the inverted uterus by a finger inserted high in the vagina. Linen sutures are placed to anchor the vaginal vault high up on the posterior wall of the uterus near the fundus. This obliterates the cul-de-sac and suspends the vaginal vault to a high point. The anterior vaginal wall is closed as usual.

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7. Fraenkel, L.: Principles of Treatment of Genital Prolapse: Technic of Ventrofixation of Vagina, Am. J. Obst. & Gynec. **13**:757-759 (June) 1927.

8. Jarcho, J.: Vaginopexy of Ventrofixation of Vagina: Simple Operation for Cure of Prolapse of Uterus and Cystocele, Clin. Med. & Surg. **35**:555-558 (Aug.) 1928.

9. Miller, Norman F.: A New Method of Correcting Complete Inversion of the Vagina With or Without Complete Prolapse: Report of Two Cases, Surg., Gynec. & Obst. **44**:550-555 (April) 1927.

10. Moschowitz, A. V.: The Pathology, Anatomy and Cure of Prolapse of the Rectum, Surg., Gynec. & Obst. **15**:7-21, 1912.

11. Jones, D. F.: Relation of the Deep Cul-de-Sac to Prolapse of the Rectum and Uterus, and to Rectocele, Boston M. & S. J. **175**:623-627 (Nov. 2) 1916.

12. Hundley, J. Mason, Jr.: Treatment of Vaginal Hernia Associated with Prolapsus Uteri, South. M. J. **20**:345-347 (May) 1927.

The usual types of colporrhaphy often serve to support the bladder and rectum, and the uterus and cervix when present. When the latter two organs are missing, simple colporrhaphy is not always successful. It is then that I would suggest the use of preserved fascia lata.

SUMMARY

An operation is described for the suspension of the prolapsed vaginal vault following panhysterectomy, and a case is reported in which successful results have been maintained for four years. The operation consists of the reconstruction of round ligaments out of preserved fascia lata of the ox and the continuation of the newly made ligaments anteriorly under the peritoneum of the bladder to give added support to that organ. It should be pointed out that building new round ligaments is more physiologic than too much mutilation of the vagina. This procedure has been used in only one case, but it is reported in the hope that other surgeons may try this technic to determine its real value.

A FORWARD GLANCE

Since strips of fascia supported a prolapsed vaginal vault, would it not be plausible to suppose that similar material would suspend a retroverted or retroflexed uterus? Not uncommonly a heavy uterus has stretched the round ligaments to thin, weak bands. Here would be a splendid place to embed strips of fascia for support.

Is it too far afield to suggest the use of Koontz' preserved fascia lata in other forms of vaginal and perineal repair, especially when the pelvic fascia has been stretched out so thin as to be of little support, often there being little more than bladder or rectal and vaginal wall from which to rebuild a good pelvic floor? In such cases it might be well to weave strips of fascia back and forth or to use a large flat piece to fill in the defect—as emphasized by Koontz.[3] Fothergill [13] emphasized in 1926 what the anatomists Elliott Smith, Cameron and Derry had pointed out:

> That the uterus, vagina and bladder are not so much suspended from above or propped up from below as they are attached by their sides where they receive their blood supply, and held in normal position by subperitoneal tissue which intervenes between the organs and the more fixed lateral structures in the pelvic floor.

Koontz' preserved fascia, either as strips or in one large piece, anchored to the lateral pelvic structures, certainly restores normal physiologic support.

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13. Fothergill, W. E.: The Development of Vaginal Operations for Genital Prolapse, Brit. M. J. **1**:273-274 (Feb. 13) 1926.